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ABSTRACTS OF WORLD MEDICINE

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ABSTRACTS OF WORLD MEDICINE

This journal is planned to provide the reader with a selection of abstracts of the more important articles appearing in medical periodicals published in different parts of the world. Comment by the abstracter, when thought necessary, is inserted between square brackets, usually at the end of an abstract. In some instances only the titles of articles are provided.

The titles of journals are given in full and also abbreviated according to the rules adopted in the *World List of Scientific Periodicals* and in *World Medical Periodicals*. The titles of articles from foreign journals are translated into English.

This journal is essentially a guide to work in progress in the world's medical centres. No abstract can be regarded as a substitute for the article abstracted. For complete information the original article must be consulted. Our aim is to give the reader sufficient details in an abstract to enable him to judge whether the original is, for him, worth reading in full.

The abstracts are grouped in broad classifications and, so far as possible, those dealing with medical and surgical aspects of the same problem appear together under the same heading. The specialist will, it is hoped, learn from this journal of work done in other fields as well as in his own. The general practitioner will be able to keep abreast of modern knowledge in the various specialties. The representation in one journal of the several aspects of Medicine will, it is believed, give an integrated picture of the whole, necessary in this age of specialization.

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ABSTRACTS OF WORLD MEDICINE

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Pathology

EXPERIMENTAL PATHOLOGY

306. **The Relationship between the Clearance and the Plasma Concentration of Inulin in Normal Man**
T. J. KENNEDY, J. KLEH, A. B. BARTOL, and D. C. DICKERSON. *Journal of Clinical Investigation* [*J. clin. Invest.*] **32**, 90–95, Jan., 1953. 8 refs.

The clearance of inulin has been studied in 14 normal subjects in experiments in which the concentration of inulin in plasma was held constant for 3 periods at each of 3 levels, about 5, 50, and 175 mg. per cent., respectively. Analysis of the data indicated that within the limits of error of the method, the clearance was identical at all plasma concentrations. These data support the conclusion that inulin is cleared at the level of glomerular filtration.—[Authors' summary.]

307. **The Function of the Eosinophile Leukocyte**
J. VAUGHN. *Blood* [*Blood*] **8**, 1–15, Jan., 1953. Bibliography.

With the advent of ACTH and cortisone the eosinophil leucocyte now occupies an important place in haematological investigation; yet its function is little understood. The granules are thought to contain a phospholipid substance and deoxyribose nucleic acid, probably with a protein centre, but no specific properties have as yet been attributed to them. It is known that the cells are phagocytic and that they play an active part in neutralizing certain toxic proteins, such as those of hydatid fluid. The present author has shown (*J. Path. Bact.*, 1952, **64**, 91) that the eosinophilia induced by the injection of a soluble, protein-free extract of *Ascaris suum* into animals which had not been exposed to any antigenic material is probably due to a direct chemical stimulation of the bone marrow by histamine or a closely related substance. In the present work, undertaken under the auspices of the East African Medical Survey and Filariasis Research, Mwanza, Tanganyika, the histological changes and distribution of eosinophils in guinea-pigs after the injection of *Ascaris* extract were compared with those following the injection of histamine and those found in naturally occurring eosinophilia.

Examination of the tissues of normal guinea-pigs with an average eosinophil count of about 100 per c.mm. showed there to be a few eosinophils in the mucosa or submucosa of the intestines, but in no other organ. After a preliminary eosinophil count, 20 unsensitized guinea-pigs were then given an injection of 30 mg. of *Ascaris* extract and were killed in groups of 4 after 1, 3, 6, 12, and 24 hours, eosinophil counts being made at 6, 12, and 24 hours, and in all cases before death. A significant rise in eosinophil count had occurred in 3 of the 4 animals killed after 3 hours, and the count rose steadily to a maximum at 12 hours, when the average in the 8 remaining animals was about 900 per c.mm. On microscopical examination of the tissues it was observed that in the larger vessels eosinophil leucocytes were arranged along the endothelium in "pavement" fashion even 1 hour after injection, and at 3 hours and later this was a common finding. An increasing number of eosinophils were seen in the perivascular connective tissue of the lungs and intestines in each group of animals. In the lungs there was an initial thickening of the alveolar capillaries and walls, associated with an emigration of eosinophil cells via the perivascular and peribronchial connective tissue to the bronchial mucosa, a few penetrating to the lumen; by 12 hours an occasional cell was seen in the parabronchial and hilar lymph nodes and spleen, and at 24 hours these were more numerous.

In 16 guinea-pigs similarly examined after the injection of 0·25 mg. of histamine the eosinophil count rose as before, but not to so high a level, the maximum being reached at 6 hours. Histologically, a picture similar to that described above was found, but with an added neutrophil leucocytosis in the alveoli, the eosinophil leucocytes appearing to have the ability to penetrate the bronchial mucosa, whereas the neutrophil leucocytes remained in the alveolar walls. Again there was a later accumulation of eosinophils in certain lymph nodes and in the spleen.

The changes accompanying naturally occurring eosinophilia were studied in only 5 guinea-pigs, their eosinophil counts being between 750 and 2,370 per c.mm. at the time of death. Histological examination showed changes similar to those described, but on a much greater scale, so that some of the lung sections showed areas of almost complete consolidation, while eosinophils were prominent in the lymph nodes and the spleen.

In discussing these results the author suggests that eosinophil leucocytes transport histamine or similar toxic substances from the bone marrow for detoxication, being extruded into the intestine, where histaminases are present, or through the lungs in cases of emergency. Thus it is suggested that the degree of eosinophilia provides an index of the release of histamine-like substances resulting from such different causes as allergic and drug reactions, helminth infestations, and malignant disease.

A. Gordon Signy

308. **Differences in the Response to Injury in Various Tissues: an Introduction to the Idea of "Fields" in Pathology**

G. R. CAMERON and R. M. L. MEHROTRA. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **65**, 1–11, Jan. 1953. 10 figs., 16 refs.

The authors describe their investigation at University College Hospital Medical School, London, into the response of various tissues of adult and immature male rats when a localized area about 28 sq. mm. in size and 0·5 to 1·0 mm. in thickness was frozen for one minute with solid carbon dioxide. In the skin of the ear and in the liver, spleen, pancreas, and voluntary muscle there was an early and intense inflammatory reaction, necrotic cells being removed rapidly and replaced by reparative tissue (3 to 7 days); in the fatty omentum, kidney, and testis the inflammatory reaction was delayed and moderate, and the rate of repair slow (28 days or more); in the adrenal gland the response was intermediate between these extremes. The implantation of frozen liver into a new environment, for example, the omentum or testis of the same animal, was followed by repair which was retarded, however, compared with that encountered when implantation was made into the natural liver environment. But after implantation of frozen testis into the liver or into the other testis the type of response and speed of replacement by fibrous tissue were similar to those seen to take place in frozen testis *in situ*. An accelerated response to local freezing resulted in immature testes, as was also the result when atrophic changes had been produced experimentally by massive dosage with oestradiol or by the induction of cryptorchidism. Freezing of the tissues produced either coagulation necrosis or cytolytic necrosis, according to the maturity of the affected tissue.

The authors consider that the phenomenon of repair depends on at least two factors: (1) the liberation from the damaged or dead cells of compounds which initiate the response to injury; and (2) the response to such agents by the mesenchymal tissues at the site of the injury. Thus variation in the response to tissue injury may be referred to either the injured cells or the cell environment, and the authors suggest that "this dual relationship represents a kind of pathological unit for which the term 'field' is suitable." *A. Ackroyd*

309. **Experimental Production of Congenital Anomalies. Timing and Degree of Anoxia as Factors Causing Fetal Deaths and Congenital Anomalies in the Mouse**

T. H. INGALLS, F. J. CURLEY, and R. A. PRINDLE. *New England Journal of Medicine* [*New Engl. J. Med.*] **247**, 758–768, Nov. 13, 1952. 8 figs., 33 refs.

The authors review factors concerned in the development of teratological anomalies, particularly the influence of chemical and mechanical trauma. They recognize that Gregg's observations upon the influence of maternal rubella has acted as a powerful stimulus to experimental teratology. The object of the present investigation, which was carried out at the Harvard School of Public Health, Boston, was to demonstrate that anoxia of the pregnant mouse caused intrauterine death or congenital deformity of the foetus, and that the effect varied with the degree of anoxia and the stage of foetal development.

Pregnant mice were placed for 5 hours in low-pressure chambers at simulated altitudes of 25,000 and 27,000 feet (7,620 and 8,230 m.). The congenital anomalies observed among the foetuses which survived included defects of the interventricular septum, anencephaly, hemivertebra and spina bifida, fused ribs, cryptorchidism, cleft palate, and open eye, in this order of onset; the incidence varied according to the stage of gestation at which the mice were subjected to the experiment and the simulated altitude employed. An interesting finding was that the body temperature of the animals fell after several hours in the chamber, suggesting that chilling was an accessory factor.

The authors discuss some clinical conditions in which anoxia may be a causative factor; for example, the relative infertility which is often found among women living in the high Andes. They also cite the case of a woman suffering from congenital heart disease who twice produced an anencephalic foetus before the cardiac lesion was operated on successfully, and who gave birth to a normal child afterwards. The authors believe that the influence of Mendelian genetics has been overemphasized. In their view neither neo-Lamarckism nor Mendelian probability provides a completely satisfactory explanation of congenital malformations. Environmental factors, which can be evaluated scientifically, operate to a far greater degree than was formerly thought, and it should be possible to devise measures to protect the fragile embryo or the vulnerable foetus.

Norman Capener

310. **Investigation of the Permeability Factor in Ascites and Edema Using Albumin Tagged with I^{131}**

J. A. SCHOENBERGER, G. KROLL, A. SAKAMOTO, and R. M. KARK. *Gastroenterology* [*Gastroenterology*] **22**, 607–622, Dec., 1952. 2 figs., 16 refs.

Exact quantitative information concerning the permeability to protein of intact vascular and serous membranes in man would be of value in testing Starling's hypothesis that an increase in this permeability is a cause of oedema. In this paper from the Research Hospital, University of Illinois, the authors describe their experimental use of human albumin labelled with radioactive iodine (^{131}I), which promises to be a useful method for the investigation *in vivo* of endothelial permeability. Mankin and Lowell (*J. clin. Invest.*, 1948, **27**, 145; *Abstracts of World Medicine*, 1948, **4**, 293) showed, in a qualitative manner, that there is a defect in membrane permeability in patients suffering from ascites, but no methods have been described for measuring the extent of this defect quantitatively. Human albumin labelled with ^{131}I, however, can be administered in tracer doses, so that the amount of albumin given has no effect on the protein equilibrium of the body and studies can repeatedly be carried out without harm to the patient.

An [unspecified] number of patients ill with ascites, oedema, and malnutrition as a result of Laennec's cirrhosis were studied, tracer doses of human serum albumin labelled with ^{131}I being injected intravenously or intraperitoneally before and during treatment with nutritious diets low in sodium. The labelled albumin moved from

the blood stream into the peritoneal cavity or vice versa, depending on the site of injection. The rapid development of radioactive equilibrium seemed to indicate that plasma albumin and ascitic-fluid albumin exist in a state of dynamic interchange and balance. The authors state that although they have shown that the " collections of ascitic fluid are not stagnant pools of briny transudate " it is still not known how albumin is transported in and out of the peritoneal cavity. They consider it reasonable to assume that the transfer of albumin to and from the ascitic fluid may involve movement across a variety of endothelial membranes, and possibly also across certain cellular membranes such as those surrounding the hepatic cells. The changes in concentration of the labelled albumin in the plasma and ascitic fluid following injection were analysed mathematically and the methods of analysis are described in detail. It was shown that from 3·86% to 4·78% of the albumin was transferred out of the circulation per hour. *E. Forrai*

311. **Intravenous Trypsin. Its Anticoagulant, Fibrinolytic and Thrombolytic Effects**
I. INNERFIELD, A. SCHWARZ, and A. ANGRIST. *Journal of Clinical Investigation* [*J. clin. Invest.*] **31**, 1049–1055, Dec., 1952. 2 figs., 20 refs.

HAEMATOLOGY

312. **A Simple and Practical Method for Measuring and Recording Blood Coagulation Time**
A. W. RICHARDSON and J. G. BISHOP. *Science* [*Science*] **117**, 37–39, Jan. 9, 1953. 6 figs., 13 refs.

With most methods of measuring the coagulation time of blood, such as the widely-used technique of Lee and White, the precision of the result may be affected by subjective errors in procedure. Moreover, Macht and Hoffmaster (*Science*, 1952, **115**, 91) showed by means of a modified Lee and White technique that coagulation is not a single event, and that a progressive series of changes occurs during the process of clotting, and this is confirmed by the fact that a progressive decrease in electrical conductivity occurs at the same time. The coagulation time as usually measured does not necessarily correspond with the end-point of this process.

The present authors have devised a method for the measurement of coagulation time in which agitation of the blood is performed mechanically, and in which the onset and completion of clotting are recorded by measuring the accompanying change in conductivity. The apparatus consists essentially of a platform which is tilted 45 degrees in each direction from the horizontal every 10 seconds by an electric motor. The platform carries a container for the blood (various patterns are described, but the authors prefer a paraffin-coated tube surrounded by a constant-temperature water-jacket) and a mercury switch which makes contact at one or other extreme of the oscillation. Electrodes are introduced through the plastic-covered cork stopper of the blood container, projecting 0·2 mm. so that fluid blood is in contact with them only when the container is tilted downwards. These electrodes are connected in series with the switch in a circuit containing a 4- or 6-volt battery, a resistance, and a recording milliammeter. When the mercury switch is placed so that it closes when the container is tilted up and the blood is not in contact with the electrodes, no current will pass until, with the onset of coagulation, contact between the electrodes is maintained by adherent clot throughout the cycle of oscillation. From then on the intermittent record shows a progressive increase in conductivity until a firm clot is established, when it remains constant (see Fig. 1).

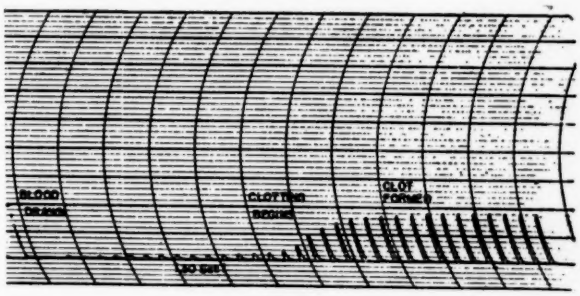

Fig. 1

Alternatively, the switch may be placed so as to close at the point in the cycle when the container is tipped downwards, the current recorded then becoming less when coagulation starts and conductivity begins to diminish, the final reading, representing the current passing through fully formed clot, being identical with that given by the first method (see Fig. 2).

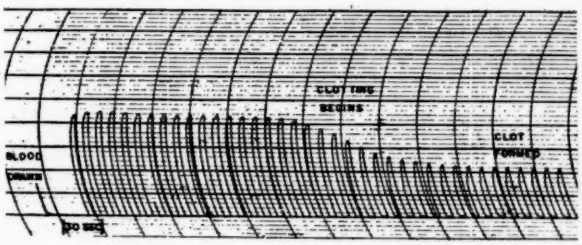

Fig. 2

The authors claim that the device is simple to make and is very practical. Taking the end-point as the point on the curve where no further change occurs, repeatable results can be obtained, the subjective errors of the Lee and White method being reduced to a minimum.
A. Gordon Signy

313. **The " Reflux " Factor in Erythrocyte Sedimentation Tests**
W. D. ALEXANDER. *British Medical Journal* [*Brit. med. J.*] **1**, 433–435, Feb. 21, 1953. 1 fig., 3 refs.

At the Gardiner Institute of Medicine (University of Glasgow) the methods of Westergren and of Wintrobe for determination of the erythrocyte sedimentation rate were compared in 40 unselected patients, the Westergren

tube being only half filled to give a comparable column of blood. In 4 cases the Wintrobe method gave normal values, and the Westergren method raised values, the latter results being those expected from the clinical picture. If, however, the Wintrobe tube was over-filled and blood then withdrawn to the zero mark so that a reflux down the sides of the tube occurred (as in the usual method of filling a Westergren tube), a reading comparable with that given by the Westergren method was obtained. Similarly, a low reading could be obtained in the Westergren tube by half-filling it with oxalated blood and preventing a reflux. With citrated blood, however, although the half-hour readings were sometimes low, the prevention of reflux had no effect on the reading at one hour.

It is tentatively suggested that the momentum gained by the blood in flowing down the sides of the tube may in part explain this phenomenon, but the main stress is laid on the practical importance of knowing that the phenomenon does occur and may affect the readings.

Marjorie Le Vay

MORBID ANATOMY AND CYTOLOGY

314. **Congenital Fibro-elastosis of the Endocardium**
N. F. C. GOWING. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **65**, 13–28, Jan., 1953. 7 figs., 44 refs.

After briefly reviewing the (mainly American) literature dealing with congenital fibro-elastosis of the endocardium, the author reports 3 cases seen at St. George's Hospital, London, in the period of one year, in one of which thrombi developed on the endocardium with resulting embolism and gangrene of both legs. He also analyses the clinical and pathological features of the disease in 76 recorded cases, including the 3 cases described in this paper.

Of these patients, 80% died within their first year, 21% dying during the first week and 29% within the first month, but the age at death ranged from 0 (stillborn) to 6½ years. Usually the patient was normal at birth and progressed satisfactorily for some time. The onset of symptoms was frequently sudden and was often precipitated by some intercurrent infection. Cardiac failure developed rapidly and was associated with a greatly enlarged globular heart; valvular lesions were inconstant. At necropsy the heart was found to be much enlarged, increased in weight, and rounded at the apex, the myocardium, especially the wall of the left ventricle, being thickened and hypertrophied and the chambers dilated. The mural endocardium, particularly on the left side, was diffusely thickened, opaque, and grey or white in colour with a smooth glistening surface, although sometimes ante-mortem thrombi were deposited on it. Deformities of the mitral or aortic valve were present in 50% of the cases.

Microscopically, between the endothelium and the myocardium there was a thick layer composed of collagenous and elastic fibres, mainly disposed parallel to the surface. A moderate number of fibrocytes were scattered amongst the fibres, but inflammatory cells were absent. In the thickened valves an increased number of spindle-shaped and stellate connective-tissue cells occurred, with an accumulation of much basophilic ground substance. Myocardial changes were inconstant, while associated congenital abnormalities occurred in less than 10% of the cases.

The author considers that the lesion represents an abnormality of cardiac development and is not caused by maternal or postnatal infection. He is also of the opinion that the endocardial sclerosis which has been described in adults represents a different disease process, and that the two conditions are not related.

A. Ackroyd

315. **Dissecting Aneurysms of the Aorta in Persons under Forty Years of Age**
I. GORE. *Archives of Pathology* [*Arch. Path.* (*Chicago*)] **55**, 1–13, Jan., 1953. 3 figs., 41 refs.

The author, in studying the pathological features of 72 cases of dissecting aneurysm of the aorta at the U.S. Armed Forces Institute of Pathology, found that the underlying degeneration in younger subjects was chiefly of the elastica, whereas in patients over 40 a corresponding change was more often found in the aortic musculature. An unusually large proportion of the 32 patients under 40 were found to have congenital defects of the cardiovascular or other systems, and as a result of this observation it is suggested that the underlying lesion in dissecting aneurysm in such cases may also be congenital in nature. This defect is possibly of a metabolic nature, since it manifests itself only after a number of years.

G. J. Cunningham

316. **Postmortem *X*-ray Studies of Congenital Malformations of the Heart**
R. M. COLLISTER, J. DANKMEIJER, H. A. SNELLEN, and W. H. VAN DER WEL. *Archives of Pathology* [*Arch. Path.* (*Chicago*)] **55**, 31–46, Jan., 1953. 9 figs.

A radiographic technique developed at the University Hospital, Leiden, for the demonstration of congenital lesions in the heart post mortem is described. Successive injections of a barium sulphate suspension are made into various portions of the heart and a series of radiographs obtained. It is claimed that this method helps in the correlation of necropsy and clinical findings and provides a suitable means of demonstrating such pathological conditions to students. Moreover, an exact knowledge of the nature of the lesion is of great assistance in deciding the best method of opening and displaying the heart.

G. J. Cunningham

317. **Malformations of the Aortic Arch System Manifested as " Vascular Rings "**
J. E. EDWARDS. *Laboratory Investigation* [*Lab. Invest.*] **2**, 56–75, Jan.–Feb., 1953. 15 figs., 23 refs.

In this paper from the Mayo Clinic, Rochester, Minnesota, in which the term " vascular ring " is defined as an anomaly of the aortic arch giving rise to symptoms of obstruction of the trachea or oesophagus, malformations of the aortic arch are discussed in relation to a hypothetical basic malformation consisting of a double

aortic arch with bilateral ductus arteriosi and a descending aorta in the midline. Any given malformation may be related developmentally to one of four variations of the basic pattern, namely, two having the ductus arteriosus and descending aorta on the same side (right or left), and two having these structures on opposite sides. The actual cases recorded are those found at necropsy at the Mayo Clinic during the years 1946–51.

There was only one case of a double aortic arch with a left ligamentum arteriosum and a left descending aorta, the two arches being of equal size. Two cases of right aortic arch with left ligamentum and left descending aorta occurred; in these cases, the right aortic arch passed dorsal to the oesophagus and gave off the left subclavian artery as its fourth branch, the ligamentum arteriosum being attached to the aorta near this artery.

The commonest malformation was an anomalous right subclavian artery, arising as the fourth branch of an otherwise normal aorta; 18 cases of this anomaly were found in a series of 3,739 consecutive necropsies. There was one case of a left aortic arch with the descending aorta lying to the right of the oesophagus. The right subclavian was the fourth branch of the aorta and arose from a diverticulum to which was attached a right ligamentum arteriosum. Another case, in which there was a tetralogy of Fallot and minimal patency of the ductus arteriosus, showed a mirror image of the normal aortic pattern (without a complete situs inversus), while a similar case showed complete absence of a ductus arteriosus. Finally, there was one case of the tetralogy of Fallot in which there was a right aortic arch and right descending aorta. The left subclavian arose as the fourth branch of the aorta, passed behind the oesophagus, and was connected to the left pulmonary artery by a patent ductus arteriosus. *D. B. Moffat*

318. **Hibernoma**
S. Gross and C. Wood. *Cancer* [*Cancer (N.Y.)*] **6**, 159–163, Jan., 1953. 4 figs., 13 refs.

It is pointed out that the so-called brown fat typically seen in hibernating mammals is also found in white rats, mice, and the human embryo. The literature contains reports of 16 instances of tumour formation of this atypical] fat (hibernoma) in human beings, and the authors, from the New York University–Bellevue Medical Center, New York, report 2 more, one of the thoracic cavity and one of the axilla.

The back, the neck, and the axilla are the usual sites of this benign, well-encapsulated tumour, which has a high unsaponifiable-fat content, and in which there is a doubly refractile substance similar to that found in the adrenal cortex. *W. Skyrme Rees*

319. **Diagnostic Significance of Fatty Cysts in Cirrhosis**
W. S. Hartroft. *Archives of Pathology* [*Arch. Path. (Chicago)*] **55**, 63–69, Jan., 1953. 4 figs., 6 refs.

It has been shown previously (Hartroft and Ridout, *Amer. J. Path.*, 1951, **27**, 951) that in animals deprived of choline fat accumulates in the parenchymal cells of the liver and that rupture of these fat-containing cells with the formation of fatty cysts is an important stage in the evolution of the cirrhosis due to choline deficiency. The cysts later lose their fat content, and the collapsed stroma forms the fibrous trabeculae seen in the fully developed disease. Similar cysts have been demonstrated in sections of the human liver in cases of alcoholic and other types of cirrhosis preceded by fatty change. In the present paper the author describes the histological findings in the liver in 95 consecutive cases of cirrhosis of all types encountered at necropsy in the Department of Pathology of the University of Toronto. He concludes that the presence of fatty cysts in areas of fibrosis is of great value in distinguishing cirrhosis following fatty change from other conditions, such as post-necrotic scarring. *G. J. Cunningham*

320. **Interpretation of Testicular Biopsy**
W. O. Nelson. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 449–454, Feb. 7, 1953. 9 figs., 8 refs.

In this paper from the State University of Iowa College of Medicine the preparation and interpretation of testicular biopsy material are discussed. Specimens should generally be about half the size of a pea, should be obtained by incision and not by punch or suction biopsy, and must be fixed immediately, preferably in Bouin's solution; formalin should not be used as a fixative.

The diagnosis of eunuchoidism usually presents the least difficulty, and the conditions found fall into three main groups. For example, of 148 eunuchoidal men examined, 62% were hypogonadotrophic, 25% showed puberal failure in development of the seminiferous tubules and Leydig cells, and 13% showed prepuberal testicular failure. The histological changes in these groups were sharply defined.

The problem of interpretation in cases of infertility is more complex, but generally these cases show a condition either of azoospermia or oligospermia. The examination of a group of 196 cases of azoospermia showed 4 main pictures: in 25% there was normal spermatogenesis, the defect being obstruction of the sperm passages; in 18% there was complete peritubular fibrosis with severe tubular damage; and 35% showed germinal-cell aplasia, the tubules being populated exclusively by Sertoli cells; the remaining 22% showed germinal-cell arrest, the point of arrest being as a rule the primary spermatocyte. In a series of 426 cases of oligospermia the findings in order of frequency were: sloughing or disorganization of the germinal epithelium (46%); incomplete germinal arrest (21%); regional or incomplete fibrosis (15%); and normal or essentially normal spermatogenesis (5%). *R. Heptinstall*

321. **Histoplasmosis, with Review of the Literature and Report of a Case, Proved by Culture, with Involvement of the Upper Lobe of Each Lung Simulating Active Bilateral Apical Pulmonary Tuberculosis**
J. Monroe and J. M. Kurung. *Annals of Internal Medicine* [*Ann. intern. Med.*] **38**, 206–223, Feb., 1953. 2 figs., bibliography

Bacteriology

322. ***Treponema pallidum* Buds, Granules, and Cysts as found in Human Syphilitic Chancres and seen in Fixed Unstained Smears Observed under Dark-ground Illumination**
W. E. COUTTS and W. R. COUTTS. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 29–36, Jan., 1953. 5 figs., 18 refs.

Within a few years of the discovery, in 1905, of the causative organism of syphilis, the presence of buds or granules attached to the body of the treponeme was described by many workers. Although these findings were considered by some to be artefacts, later investigations, particularly by electron microscopy, confirmed the existence and frequent occurrence of such structures. The part, if any, played by these buds in the life cycle of *Treponema pallidum*, and of other spirochaetes in which they occur, has been the subject of much conjecture.

The present authors, working in the Department of Public Health, Santiago, Chile, studied these structures by dark-field microscopy in dried unstained films of serum from cases of syphilitic chancre. They describe various forms of bud attached to the treponeme and also free, spherical bodies of varying density, some of which contained a comma-shaped structure. The latter were noted in serum from syphilitic chancres and in fluid aspirated from enlarged syphilitic lymph nodes in which no treponemes were found.

The authors discuss these observations in relation to theories concerning the life cycle of *T. pallidum*; while believing in the existence of a life cycle, they find it impossible to establish a definite correlation between the various phases observed. *V. E. Lloyd*

BACTERIA

323. **A Study of the Neutral Red Reaction for Determining the Virulence of Mycobacteria**
W. C. MORSE, M. C. DAIL, and I. OLITZKY. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **43**, 36–39, Jan., 1953. 6 refs.

The authors report their experience of the method of determining *in vitro* the virulence of tubercle bacilli (Dubos and Middlebrook, *Amer. Rev. Tuberc.*, 1948, **58**, 698) in which an alkaline buffered aqueous solution of neutral red is added to a suspension of mycobacteria washed in methyl alcohol. Virulent strains bind the dye and are stained pink or red. A good correlation was observed between the results of guinea-pig inoculation and the results of the dye tests, both being positive in 163 cases and both negative in 3, with strains of *Mycobacterium tuberculosis*. In addition 12 acid-fast chromogens gave negative results by both methods.

There were, however, some notable exceptions. With 2 strains of tubercle bacilli a positive result was obtained *in vitro*, but the organisms failed to infect the guinea-pig; subsequent investigations proved that these strains were avian variants. One human, 1 bovine, and 2 avian lyophilized laboratory stock cultures likewise gave a positive result *in vitro*, but were avirulent for laboratory animals. *R. Salm*

324. **The Virulence of Tubercle Bacilli Resistant to PAS.** (Sulla virulenza dei micobatteri tubercolari P.A.S.-resistenti)
V. NITTI and E. TALIERCIO. *Archivio di tisiologia* [*Arch. Tisiol.*] **7**, 974–980, Dec., 1952. 5 refs.

The authors briefly review the earlier reports of loss of virulence by tubercle bacilli which became streptomycin-resistant or streptomycin-dependent, and describe their own work carried out at the Principi di Piemonte Sanatorium, Naples, with PAS-resistant strains to determine whether strains resistant to chemical therapeutic agents behaved similarly to streptomycin-resistant strains. The strain of tubercle bacillus used was a variety of H37Rv which by successive subcultures in PAS-containing media had become resistant and which they have designated H37P/R. Three groups, each of 12 guinea-pigs, were inoculated with a standard emulsion of bacilli, the first group being given H37P/R and no treatment, the second H37P/R and being treated with PAS, and the third group being inoculated with H37Rv as a control. Some of the guinea-pigs in each group were examined after 35 days and the rest at 90 days.

Details of the subsequent histological and bacteriological examinations are given. In the groups inoculated with Strain H37P/R the lesions were more localized and no death from generalized tuberculosis occurred. In the group inoculated with Strain H37Rv, 6 animals died from tuberculosis before 90 days and the remainder showed typical progressive tuberculous lesions. The strains were also tested with the authors' own modification of Dubos's neutral-red reaction; the PAS-resistant strains behaved like other resistant strains and not like the virulent H37Rv.

The authors conclude that PAS-resistant strains of tubercle bacilli show a marked loss of virulence similar to that of strains resistant to other antibacterial agents.
R. F. Jennison

325. **Anaerogenic Paracolon Bacilli Associated with Gastro-enteritis in Children**
G. W. BROWN. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 658–663, Nov. 8, 1952. 32 refs.

The general biochemical characters of the anaerogenic paracolon bacilli are similar to those described by Stuart *et al.* (*J. Bact.* 1943, **45**, 101) for a paracolon type of organism associated with cases of gastro-enteritis, but their antigenic formulae are different.

In an investigation at the Children's Hospital, Adelaide, the author isolated strains of this anaerogenic type

from the stools of 13 young children suffering from gastro-enteritis, but she failed to find similar types in the stools of 100 control children. The biochemical and antigenic characters of 12 of the strains were identical, while the remaining strain, although related, exhibited some differences. Complete serological investigations were not carried out, but both types possessed a heat-labile surface antigen having similar properties to the α-antigen of Stamp and Stone which was not, however, specifically identified. The heat-stable O antigens were not identical but the H antigens were similar. The serum of a significant number of the patients from whom these organisms were isolated was found to possess specific agglutinins for these organisms, and on these findings the author assumes that the types were pathogenic.

Stuart *et al.* have shown that the paracolon bacillus Type 29911, to which these organisms have some relation, forms a serologically heterogeneous group ; it therefore seems reasonable to include in the same group the paracolon bacilli isolated by the author. *H. J. Bensted*

326. **A New Salmonella Type of Human Origin: *Salm.* Bolton**
E. Greenwood, A. Powis, S. H. Douglas, and J. Taylor. *Monthly Bulletin of the Ministry of Health* [*Monthly Bull. Minist. Hlth (Lond.)*] **12**, 29, Jan., 1953.

327. **A New Salmonella Type of Human Origin: *Salm.* Nottingham**
G. B. Ludlam, J. Taylor, and S. H. Douglas. *Monthly Bulletin of the Ministry of Health* [*Monthly Bull. Minist. Hlth (Lond.)*] **12**, 29–30, Jan., 1953.

VIRUSES

328. **Attempts to Demonstrate Interference between Coxsackie and Poliomyelitis Viruses in Mice and Monkeys**
N. F. Stanley. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **81**, 430–433, Nov., 1952. 1 fig., 4 refs.

The experiments described in this paper were carried out at the Prince Henry Hospital, Sydney, with the aim of investigating the occurrence of interference between Coxsackie and poliomyelitis viruses when the two were inoculated simultaneously into mice. It was found that when a mixture of Group-A Coxsackie virus and MEF1 strain of poliomyelitis virus was inoculated intracerebrally into adult mice the incubation period of the poliomyelitis virus decreased ; with Group-B Coxsackie virus, however, the inoculation period increased. No similar effect was demonstrated in monkeys when a strain of poliomyelitis virus was used which had been freshly isolated from the spinal cord in a fatal case of human poliomyelitis.

An interesting feature of the investigation with the MEF1 strain of poliomyelitis in mice was the persistent demonstration of two peaks in a graph in which the time of onset of paralysis was plotted against the number of animals becoming paralysed. Further experiments showed that viraemia was present in these animals only for a short time about 24 hours before the time indicated by the peaks in the graph. *Peter Story*

329. **Studies on the Cultivation of Poliomyelitis Viruses in Tissue Culture. I. The Propagation of Poliomyelitis Viruses in Suspended Cell Cultures of Various Human Tissues**
T. H. Weller, J. F. Enders, F. C. Robbins, and M. B. Stoddard. *Journal of Immunology* [*J. Immunol.*] **69**, 645–671, Dec., 1952. 5 figs., 22 refs.

This paper, from the Children's Medical Center and Harvard Medical School, Boston, describes the technique employed by which the Lansing, Brunhilde, and Leon strains of poliomyelitis virus were shown to be capable of multiplication in suspended cell cultures of human embryonic skin, muscle, brain, and intestinal tissue, and of mature human kidney tissue. Other tissues such as embryonic thyroid, and adrenal, spleen, prepuce, and testis were also employed, but the most suitable were embryonic skin, muscle, kidney, and brain tissues. The technique employed [which is complicated and for which the original paper should be consulted] is based on the observation that about 12 or more days are required before the virus increases in titre to any great extent. Its most important features are the replacement of the nutrient fluids by fresh fluid at intervals of 3 or 4 days and the infrequent passage of the developing virus to new cultures.

That growth of the virus had occurred was proved by titration in animals, and also by evidence of damage sustained by the cells owing to the presence of the virus. This included a fall in the *p*H of the suspending fluid, a difference in *p*H of 0·2 between infected and control tubes being considered significant, the failure of infected tissues to multiply when transferred to suitable media, and degeneration of the growing cells in roller-tube cultures. The Lansing strain was maintained for 23 passages over a period of 331 days, and the Brunhilde strain for 15 passages over 267 days. There was evidence that the infectivity of both strains was diminished in the course of cultivation *in vitro*. *R. Hare*

330. **Studies on the Cultivation of Poliomyelitis Viruses in Tissue Culture. II. The Propagation of the Poliomyelitis Viruses in Roller-tube Cultures of Various Human Tissues**
F. C. Robbins, T. H. Weller, and J. F. Enders. *Journal of Immunology* [*J. Immunol.*] **69**, 673–694, Dec., 1952. 5 figs., 24 refs.

In these further experiments [see Abstract 329] roller-tube cultures of human embryonic skin or muscle, of mature human uterus, kidney, testis, or prepuce, and of monkey kidney or testis were all employed for the cultivation of Lansing, Brunhilde, and Leon strains of poliomyelitis virus; the technique is described in considerable detail. The experiments show that there is no doubt that the virus will multiply in extraneural tissues and over a considerable number of passages. Indeed,

on some occasions, the yield of Lansing virus in the fluid equalled, or even exceeded, the titres usually obtained in the brains of infected mice.

The authors point out that roller-tube cultures have certain advantages compared with suspended-cell cultures: the degeneration of the cells (which may be used as an indicator of growth of the virus) can be observed directly, the growth of virus is more rapid, and more tubes can be made from the same amount of tissue. The disadvantages of the method are the rather more elaborate equipment required, the more difficult technique, and the more complex medium. *R. Hare*

331. **Interference between Japanese B Encephalitis Virus and Western Equinine Encephalomyelitis Virus in the Rat**

C. E. DUFFY, G. C. PEHRSON, and P. N. MORGAN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **81**, 154–157, Oct., 1952. 6 refs.

The purpose of this investigation, carried out at the University of Arkansas, Little Rock, was to determine whether Japanese B encephalitis virus, which, like St. Louis encephalitis (S.L.E.) virus, produced a fatal infection in a 7-day-old but not in a 21-day-old rat, prevented infection with Western equine encephalomyelitis (W.E.E.) virus on intranasal inoculation of both viruses, since S.L.E. virus interferes in this way with W.E.E. virus and may prevent an otherwise fatal infection.

Japanese B encephalitis virus was instilled into the nose of 21-day-old rats 72 hours before inoculation with W.E.E. virus by the same route. If one inoculation of Japanese B virus preceded the W.E.E. virus, 50% of the rats survived, whereas 67% survived if 3 inoculations of Japanese B virus were given. All the control animals died. The protection afforded against W.E.E. virus by previous inoculation with Japanese B virus was short-lived in nearly every case. Survivors of the first test were inoculated 23 days later with W.E.E. virus and nearly all died. *Peter Story*

SEROLOGY AND IMMUNOLOGY

332. **Complement Fixation with the Three Types of Poliomyelitis Viruses Propagated in Tissue Culture**

A. SVEDMYR, J. F. ENDERS, and A. HOLLOWAY. *American Journal of Hygiene* [*Amer. J. Hyg.*] **57**, 60–70, Jan., 1953. 15 refs.

For an investigation, at the Children's Medical Center and Harvard Medical School, Boston, of the serological response in human beings to the viruses of poliomyelitis, antigens for a complement-fixation (C.F.) test were prepared by inoculation of tissue cultures of human embryonic skin and muscle or mature kidney tissue with Lansing, Brunhilde, or Leon type virus. The C.F. test was carried out by a drop method. Serum from monkeys infected intramuscularly or intracerebrally reacted only with homologous virus; this high degree of specificity was not found in human serum. Tests were carried out with serum from 24 patients with poliomyelitis from whose stools Brunhilde-type (16 cases) or Leon-type virus (8 cases) had been isolated. In all cases convalescent sera gave C.F. titres of not less than 8 against at least one antigen. Homologous C.F. antibody in this range and homologous virus-neutralizing antibody were both present in 22 cases and both absent in 2 cases. In 10 of the positive cases, 9 with Brunhilde virus and 1 with Leon virus, there was a significant increase in titre (not less than fourfold) against the homologous antigen; the titre in the other 12 cases was high initially and did not rise significantly. The sera of all convalescent patients fixed complement to some degree in the presence of heterologous virus, but about half gave negative results in neutralizing-antibody tests against heterologous virus. The C.F. titres of the sera remained at the same level for at least one month and fell significantly after 1½ to 3 years.

The authors suggest that poliomyelitis viruses contain type-specific and group antigens. The C.F. test is of limited value as a diagnostic aid, because in many cases the maximum level of C.F. antibody is attained very early. Only exceptionally can the type of virus be identified with confidence by this test. *M. Lubran*

333. **Experimental Studies on Passive Immunization against Poliomyelitis. II. The Prophylactic Effect of Human Gamma Globulin on Paralytic Poliomyelitis in Cynomolgus Monkeys after Virus Feeding**

D. BODIAN. *American Journal of Hygiene* [*Amer. J. Hyg.*] **56**, 78–89, July, 1952. 25 refs.

In a previous paper (*Amer. J. Hyg.*, 1951, **54**, 132) the author reported the striking prophylactic effect of gamma globulin against paralysis due to intramuscular inoculation of poliomyelitis virus in rhesus monkeys. Further investigations have been carried out at the Johns Hopkins University, Baltimore, into the effect of gamma globulin as a prophylactic agent when the virus is administered by mouth. Young cynomolgus monkeys, some of which had received shortly beforehand an intramuscular injection of human gamma globulin, were given poliomyelitis virus orally. The following five strains of the virus, representing three types, were used: Per, Y-SK, Leon, Mahoney, and Wallingford. The paralysis rate was highest after administration of the Mahoney strain, and this strain was therefore used in the subsequent experiments.

In 7 experiments in which the passive serum antibody titre, as judged by mouse protection tests, ranged from 1 in 100 to 1 in 2, none of the 58 animals developed paralysis, compared with 23 out of 57 controls. In 2 groups, each of 10 monkeys, in which the antibody titre was 1 in 1 or less, there was no significant protection, though the incubation period was prolonged.

It is believed that the presence of specific serum antibody above a critical titre prevents the onset of paralysis when the virus is given by mouth. These results would seem to bear significantly on both passive and active immunization against poliomyelitis and the level of circulating antibody needed to ensure protection.

G. Payling Wright

Pharmacology

334. **Response in Dogs to Relaxants Derived from Succinic Acid and Choline**
L. W. HALL, H. LEHMANN, and E. SILK. *British Medical Journal* [*Brit. med. J.*] **1**, 134–136, Jan. 17, 1953. 4 refs.

Since dogs are more sensitive to suxethonium than man, the authors, working at the Royal Veterinary College and St. Bartholomew's Hospital, London, carried out an investigation to determine whether this indicated a difference between the enzyme systems of man and the dog. Both suxethonium dibromide and suxamethonium chloride were used in experiments *in vivo* and *in vitro*. There was no major difference in their behaviour. In experiments *in vitro*, the activity of the enzymes was expressed as μl. of CO_2 liberated per minute from a bicarbonate buffer by 1 ml. of serum or packed erythrocytes at 37° C.

In 25 operations on dogs suxethonium was given in dosages ranging from 0·08 to 0·15 mg. per lb. (0·2 to 0·3 mg. per kg.) body weight. In man 4 to 6 times these doses were given, yet the apnoea lasted longer in the dog. It was established that in dogs as in man suxamethonium and suxethonium inhibit the hydrolysis of acetylcholine by both the true cholinesterase from the erythrocytes and the pseudocholinesterase of the plasma; and further that the two drugs themselves are hydrolysed by pseudocholinesterase. While it might have been expected that the pseudocholinesterase level would be lower in the dogs than in man, the difference was found to be slight; on the other hand, the true cholinesterase level was found to be much lower in the dog.

The action of succinylcholine may be explained by regarding the free drug and its combination respectively with true cholinesterase (pharmacologically active) and with pseudocholinesterase (unstable) as forming a system in equilibrium, deficiency of true cholinesterase resulting in an increased availability of the free drug which can be hydrolysed by the pseudocholinesterase. In 5 dogs the injection of a pseudocholinesterase preparation effectively shortened the period of apnoea after administration of suxethonium or suxamethonium.

The theoretical and practical significance of these findings is discussed. [See also Abstract 335.]

Norval Taylor

335. **Effect of Pseudocholinesterase Level on Action of Succinylcholine in Man**
F. T. EVANS, P. W. S. GRAY, H. LEHMANN, and E. SILK. *British Medical Journal* [*Brit. med. J.*] **1**, 136–138, Jan. 17, 1953. 9 refs.

In an investigation at St. Bartholomew's Hospital, London, into the effect of the blood pseudocholinesterase level on the action of succinylcholine, pseudo- and true cholinesterase levels were estimated in serum and laked and washed erythrocytes respectively. The activity of the enzymes was assessed by measuring the CO_2 liberated from a bicarbonate buffer by the products of enzyme hydrolysis, expressed as μl. of CO_2 formed per minute by 1 ml. of serum or packed erythrocytes at 37° C.

Thiopentone was given to 4 patients and a sample of blood taken. Succinylcholine chloride (50 mg.) was then injected, and the period of apnoea measured with a stopwatch. When breathing was re-established a proprietary pseudocholinesterase preparation ("cholase") was injected intravenously and after 90 seconds a further sample of blood was taken. Succinylcholine was again injected and the period of apnoea measured as before. The injection of pseudocholinesterase was found to shorten the apnoeic response to succinylcholine. Not all the pseudocholinesterase injected could be recovered in the plasma; 20,000 to 50,000 units leaked into the tissues in a few minutes. None of the enzyme was found in the urine. [See also Abstract 334.] *Norval Taylor*

336. **The Influence of Barbiturate on the Sympathetic Nervous System**
E. R. TRETHEWIE. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 100–104, Jan. 24, 1953. 4 figs., 15 refs.

From the University of Melbourne the author reports the results of three different experiments in which the effect of barbiturates in depressing the sympathetic response in animals and in causing changes in the skin temperature and basal metabolic rate in man was investigated. In the first experiment records were taken of the blood pressure in an unspecified number of anaesthetized cats in which the vagus nerves were cut. Stimulation of the splanchnic nerve resulted in vasoconstriction in the splanchnic area in animals in which the adrenal glands had been removed, and general vasoconstriction, with, in addition. release of adrenaline–noradrenaline, in intact animals. Administration of a large dose of pentobarbitone sodium (25 mg. per kg. body weight) markedly lowered the blood pressure and diminished the pressor response to the stimuli.

In the second experiment records were taken of the skin temperature of the arms and feet of 3 patients, kept in bed under comfortable conditions, before and after the oral administration of phenobarbitone or pentobarbitone. In all cases a rise in skin temperature was obtained for prolonged periods, indicating increased peripheral blood flow in the skin of the limbs, this being attributed to inhibition of sympathetic tone. In the third experiment the basal metabolic rate was estimated in 4 patients before and after barbiturate was given by mouth; it was found in all cases to have fallen.

It is argued that a fall in the basal metabolic rate in the presence of normal sympathetic function ought to produce vasoconstriction. Since the rise in skin tem-

perature indicated vasodilatation and the animal experiments indicated a lessened response to splanchnic stimulation, this vasodilator effect in man is thought to be due to a blockage both of ganglionic transmission and neuromuscular transmission [but this assumption is hardly justified on the evidence presented]. The significance of these findings in relation to the treatment of hypertension is discussed. *James D. P. Graham*

337. **Correction by a Disubstituted Urea of Respiratory Depression during Experimental Narcosis with Barbiturates.** (Correction par une urée disubstituée (" 1064 Th ") de la dépression respiratoire au cours de la narcose expérimentale par les barbituriques)
D. Bargeton, M. Éon, and C. Krumm-Heller. *Archives internationales de pharmacodynamie et de thérapie* [*Arch. int. Pharmacodyn.*] **91**, 404–411, Sept. 15, 1952. 3 figs., 4 refs.

The respiratory depression produced by hexobarbitone or thiopentone in rabbits is reduced, abolished, or even changed to stimulation by the intravenous injection of a disubstituted urea compound, " 1064 Th " (N: N -di-*n*-butyl-N: N′-biscarboxymorpholide ethylenediamine), in doses of 0·25 to 0·50 mg. without altering the depth or duration of narcosis due to the barbiturate. It appears to have a high therapeutic index, the dose required to correct respiratory depression in the rabbit being about one-fortieth of that which causes convulsions.
Derek R. Wood

338. **Phenylethylacetylurea. Its General Pharmacological Properties and Comparison with Other Anticonvulsant Drugs.** (La phényléthylacétylurée. Propriétés pharmacodynamiques générales et comparaison de ce corps avec d'autres anti-épileptiques)
P. Gold, E. Frommel, C. Radouco, G. Greder, D. Melkonian, R. Della Santa, S. Radouco, F. Vallette, and M. Ducommun. *Archives internationales de pharmacodynamie et de thérapie* [*Arch. int. Pharmacodyn.*] **91**, 437–460, Sept. 15, 1953. 6 figs., 12 refs.

The anticonvulsant activity and other properties of phenylethylacetylurea (" S. 46 ") and of " M.551 ", which is a mixture of 5 parts of phenylethylacetylurea with 1 part of phenylacetylurea, in experimental animals have been studied by the authors at the University of Geneva.

Both of these preparations protected animals against chemically and electrically induced convulsions, but without any sedative effect—there was even some slight central stimulation. Again, unlike phenobarbitone, anticonvulsant doses of these drugs did not depress respiration in rabbits. Neither S.46 nor M.551 had any effect on the blood pressure, electrocardiogram, or body temperature, nor on the concentration of glucose, calcium, or inorganic phosphate in the blood. As an antagonist of the contractions of isolated guinea-pig ileum induced by histamine, acetylcholine, and barium chloride, phenylethylacetylurea was more effective than phenobarbitone, but less so than phenytoin. It also conferred on guinea-pigs some protection against bronchospasm due to acetylcholine, but not against that due to histamine. Anticonvulsant activity in guinea-pigs and rabbits was maximal about 3 to 5 hours after a single oral dose of either preparation, but was absent after 24 hours. There appeared to be no cumulation of anticonvulsant action when doses were repeated daily for 24 days. After large daily oral doses of S.46 or M.551 for 90 days the authors found no significant changes in the peripheral blood or bone marrow of guinea-pigs, nor usually in other body tissues; but in some animals given M.551 in doses of 48 mg. per kg. body weight daily they found histological evidence of liver damage, which they attribute to the phenylacetylurea in the mixture.

[The general impression given is that phenylethylacetylurea is less toxic, has fewer side-effects and other actions, and has a less prolonged anticonvulsant effect, with less danger of cumulation, than phenobarbitone.]
Derek R. Wood

339. **The Cough Alleviating Effect of β-(Diphenylmethoxy)-ethyl-trimethylammoniumbromide.** [In English]
L. A. Hahn and H. Wilbrand. *Archives internationales de pharmacodynamie et de thérapie* [*Arch. int. Pharmacodyn.*] **91**, 144–150, Sept. 1, 1952. 8 refs.

β - (Diphenylmethoxy) - ethyl - trimethylammoniumbromide not only has powerful antihistamine properties, but also antagonizes the action of stimulants of the central nervous system and prolongs the anaesthetic effect of barbiturates in mice. At the Pharmacological Institute, University of Uppsala, in human volunteers in whom cough was induced by inhalation of ammonia, 10 to 20 mg. of this quarternary compound had an effect on the cough threshold comparable to that of the same dose of codeine phosphate. There was no summation of its action with that of codeine or methadone and the compound did not depress the respiration.
Derek R. Wood

340. **The Effect of Intravenous Injection of Emulsified Vitamin K_1 on the Hypoprothrombinemia Induced by Tromexan**
W. C. Van Buskirk. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 57–58, Jan. 8, 1953. 1 fig., 13 refs.

Since vitamin K will reverse the hypoprothrombinaemia induced by dicoumarol, it seemed possible that it might have the same effect on that induced by " tromexan " (ethyl biscoumacetate) and this possibility was investigated by the author at the Veterans Administration Hospital, West Roxbury, Massachusetts. Of 18 patients who had been given sufficient tromexan to reduce the plasma prothrombin level to 10 to 30% of normal, 10 were given an intravenous injection of an emulsified preparation of vitamin K_1—the purified, naturally occurring compound identical with that originally isolated by Dam and his associates—in a dosage of 5 mg. per kg. body weight over a period of 15 minutes, 2 received 75 mg. of " synkayvite " (a water-soluble naphthoquinone with vitamin-K activity) intravenously in doses of 15 mg., while 6 others received no tromexan antagonist. The injections were given in all cases 16 hours after the last dose of tromexan, when the plasma

prothrombin level was stable. In those treated with the emulsion the prothrombin level had risen to double its original value and outside the therapeutic (or dangerous) range within 3 hours (19 hours after the last dose of tromexan), and after 24 hours it averaged 73·2% of the normal, whereas in the 6 control cases the average prothrombin level was still well within the therapeutic range 24 hours after the last dose of tromexan, and 16 hours later it was only 50·5% of normal. The results in those patients given synkayvite were similar to those of the control group. No untoward effects resulted from the intravenous administration of the emulsion of vitamin K_1. *Robert Hodgkinson*

341. **The Effect of Intravenously Administered 6063, the Carbonic Anhydrase Inhibitor, 2-Acetylamino-1 : 3 : 4-thiadiazole-5-sulfonamide, on Fluid and Electrolytes in Normal Subjects and Patients with Congestive Heart Failure**

C. K. FRIEDBERG, M. HALPERN, and R. TAYMOR. *Journal of Clinical Investigation* [*J. clin. Invest.*] **31**, 1074–1081, Dec., 1952. 4 figs., 31 refs.

This paper from the Mount Sinai Hospital, New York, gives an account of the effects of intravenous administration of 2-acetylamine-1:3:4-thiadiazole-5-sulphonamide (" 6063 "), a carbonic anyhydrase inhibitor, on water and electrolyte excretion and the blood electrolyte levels in 15 subjects (10 men and 5 women). Three of these acted as controls, being free from renal or cardiovascular disease, whereas the remaining 12 were suffering from congestive heart failure of varied aetiology, though only one showed evidence of oedema. The daily salt intake of 2 of the controls and 4 of the patients was 5 to 7 g., that of the remainder being restricted to 0·2 to 0·5 g. All were well hydrated before and during the experiment. The dose of 6063 given was 750 mg. in 250 ml. of 5% dextrose except for one patient, who weighed only 42·3 kg. and received 400 mg.

An increase in urinary output and a decrease in body weight were the usual effects of the injection, the latter ranging from 0·5 to 2·7 kg. in 24 hours. The urine became alkaline within 30 minutes of the administration of 6063, the *p*H reaching a maximum figure of 7·7 within 2 hours. Ammonia excretion was diminished, but never abolished, whereas bicarbonate excretion increased considerably. The blood bicarbonate level and *p*H showed only a slight tendency towards acidosis, but this was more marked in other patients studied who were given the drug by mouth for several days. Sodium, potassium, and bicarbonate were excreted in greater quantities than normal in both experimental and control subjects. No toxic effects were noted. The effects of 6063 and a mercurial diuretic were compared in 2 patients whose clinical state was essentially similar; the onset and peak of the effect of the former occurred earlier, but the increase in urinary flow was less than with the mercurial; excretion of sodium and chloride was markedly increased after the mercurial and less so after 6063, whereas the reverse was the case in respect of bicarbonate.

The mechanism of the diuretic action of 6063 is considered to be a limitation of the reabsorption of sodium and bicarbonate ions in the distal part of the tubules, even in patients with congestive heart failure; the inhibition of hydrogen-ion release into the tubules is thought to account for the diminished excretion of ammonia. *A. T. Macqueen*

342. **Action of Salicylates and Related Drugs on Inflammation**

G. UNGAR, E. DAMGAARD, and F. P. HUMMEL. *American Journal of Physiology* [*Amer. J. Physiol.*] **171**, 545–553, Dec., 1952. 3 figs., 32 refs.

The authors, working at the North-western University, Chicago, have studied the action of salicylates on inflammation. Instead of using a chemical irritant to produce inflammation, they made use of the Arthus phenomenon, which was induced in guinea-pigs by intracardiac injection of anti-egg-albumen rabbit serum, followed by intra-articular injection of egg albumen. The diameter of the injected joint was measured at 30-minute intervals for 5 hours. The effect on the swelling of injection of the drug intraperitoneally 1 hour before injection of the egg albumen was expressed as the " swelling index "—that is, the swelling in treated animals calculated as a percentage of the swelling in untreated controls.

Salicylates and related compounds which contain an *o*-hydroxyl group inhibited swelling: *m*- and *p*-hydroxyl derivatives did not. Salicyl alcohol was active in proportion to the serum salicylate level produced by its conversion to salicylate, but salicyluric acid, in which the carboxyl group is not easily dissociable, was inactive. Phenazone (" antipyrine "), amidopyrine, phenacetin, *p*-aminophenol, and 3-hydroxy-2-phenylcinchoninic acid were active; acetylsalicylic acid was active when given by mouth.

The part played by endocrine activity in the development of inflammation was studied in rats. Filtered egg-white was injected subcutaneously into the dorsum of one foot, and the swelling compared with that produced by injection of an equal volume of saline in the opposite foot. Salicylate caused depletion of adrenal ascorbic acid in normal rats but not in hypophysectomized animals. However, the reduction of swelling of the foot was substantially the same in normal and hypophysectomized rats; the authors therefore consider that the anti-inflammatory action of salicylate is exerted directly upon the affected tissues. They tested this hypothesis by studying the inhibitory effect of drugs upon fibrinolysin *in vitro*. They found a direct correlation between anti-inflammatory action and inhibition *in vitro* of fibrinolysin with drugs such as salicylate, phenazone, and *p*-aminophenol, the concentration of salicylate which inhibited fibrinolysin *in vitro* being of the same order as the blood level required for anti-inflammatory action *in vivo*. No activity *in vitro* or *in vivo* was found with benzoic acid, *m*- or *p*-hydroxybenzoic acid, or salicyluric acid. A third group of drugs, which included acetylsalicylic acid, salicyl alcohol, phenacetin, and acetanilide, were active *in vivo* but not *in vitro*, and these compounds are known to be metabolized into active substances such as salicylate or *p*-aminophenol. *L. G. Goodwin*

Chemotherapy

343. **Clinical Studies on Triethylenephosphoramide and Diethylenephosphoramide, Compounds with Nitrogen-mustard-like Activity**
M. P. SYKES, D. A. KARNOFSKY, F. S. PHILIPS, and J. H. BURCHENAL. *Cancer* [*Cancer* (*N.Y.*)] **6**, 142–148, Jan., 1953. 15 refs.

DEPA and TEPA, diethylene- and triethylene-phosphoramide respectively, inhibit the growth of animal tumours and cause pathological effects similar to those produced by nitrogen mustard and some of its derivatives. DEPA and TEPA are about one-tenth as active by weight as triethylenemelamine. TEPA, the principal agent used in this clinical study, is available in peanut oil for intramuscular injection. The average adult dose in a course of treatment is in the range of 80 to 120 mg. (1·2 to 2·0 mg. per kg.) given in four to six divided doses over a two-week period. As with HN_2 and TEM, TEPA produces bone-marrow depression, and this is the chief hazard associated with its use.

Nine patients were treated with DEPA and 28 with TEPA. Evidences of therapeutic activity were seen in Hodgkin's disease, lymphosarcoma, chronic lymphatic leukemia, mycosis fungoides, and in an unusual case of metastatic leptomeningeal sarcoma. As far as can be determined, however, from our limited data obtained almost entirely on patients with far-advanced diseases, TEPA did not appear to produce any benefit in patients who would not be expected to respond to HN_2 or TEM. Therefore, there do not appear to be any important indications for TEPA when compared with HN_2 or TEM. However, an effective intramuscular preparation of a compound with nitrogen-mustard-like activity may facilitate the management of an occasional patient.—[Authors' summary.]

344. **Clinical Studies on the Carcinolytic Action of Triethylenephosphoramide**
S. FARBER, R. APPLETON, V. DOWNING, F. HEALD, J. KING, and R. TOCH. *Cancer* [*Cancer* (*N.Y.*)] **6**, 135–141, Jan., 1953. 15 refs.

The authors describe the results of administration of triethylenephosphoramide (TEPA) in the Pathology Department, Harvard Medical School, in 69 cases of widespread cancer not amenable to surgery or radiotherapy. The patients' ages ranged from 7 months to 73 years. TEPA was given orally suspended in olive oil in gelatin capsules, each capsule containing either 5 or 10 mg., or intramuscularly in a 1 or 2% suspension in peanut or sesame oil, or by both routes. The daily dose varied from 0·5 to 25 mg. With two exceptions the average total effective dose was 2·1 mg. per kg. body weight. The effect of the drug was observed between 7 and 89 days after treatment started, the average daily dose until response was noted being 0·27 mg. per kg. body weight, with a range of 0·04 to 1·24 mg.

There was no improvement in 54 patients. In 11 children with acute leukaemia there was a fall in the leucocyte count, but the effect on the clinical condition was not comparable with that produced by treatment with folic acid antagonists or cortisone and ACTH. In one out of 2 cases of chronic myelogenous leukaemia there was a transitory fall in the leucocyte count. In one case of undifferentiated carcinoma there was regression in the size of the primary growth and of the metastases, but the patient died from intercurrent infection with leucopenia. There was definite improvement in 4 out of 9 cases of neuroblastoma. Of 2 patients with Hodgkin's disease one improved, while 2 out of 8 with melanoma responded well, the disease being controlled with small maintenance doses.

The chief toxic effect of TEPA was bone-marrow depression, leading to leucopenia and thrombocytopenia in almost half the patients. The authors recommend an initial daily intramuscular injection of 0·15 to 0·20 mg. per kg. body weight unless the patient is old or has had previous *x*-ray or nitrogen-mustard therapy, when the dose should be reduced. Leucocyte and platelet counts should be performed on alternate days. If gastro-intestinal symptoms develop or there are signs of marrow depression, treatment should be discontinued until the blood picture improves. In further treatment the dose should be reduced. *H. F. Reichenfeld*

345. **The Treatment of Human Cancer with Intra-arterial Nitrogen Mustard (Methylbis-(2-chloroethyl) Amine Hydrochloride) Utilizing a Simplified Catheter Technique**
R. D. SULLIVAN, R. JONES, T. G. SCHNABEL, and J. M. SHOREY. *Cancer* [*Cancer* (*N.Y.*)] **6**, 121–134, Jan., 1953. 14 figs., 32 refs.

The authors, working at the University of Pennsylvania, Philadelphia, describe the results of intra-arterial nitrogen-mustard therapy in 6 cases of carcinoma, 4 cases of lymphoma, and 2 cases each of melanoma and sarcoma. All the patients had previously received irradiation or nitrogen mustard intravenously and had ceased to respond to this treatment.

A polyvinyl catheter which had been impregnated with barium sulphate was first treated with heat or ether to render it more easily manipulated, and a three-way stop-cock was attached to the proximal end. The catheter was introduced through a 19- or 21-gauge needle into the nearest available artery. After the needle was withdrawn, pressure was applied until haemostasis was achieved. The catheter was then advanced under radiological control either distally or proximally according to the site of the tumour. After testing for patency by the injection of normal saline, nitrogen mustard was administered either in single or divided doses, the dosage varying between 0·3 and 3·8 mg. per kg. body weight.

The only complications of the technique were partial thrombosis of the artery in 2 cases and complete thrombosis in one.

Some degree of leucopenia was noticed in all patients, while in 4 of the 6 patients who received a dose of more than 1·0 mg. per kg. the leucocyte count fell to 200 per c.mm. between the 13th and 22nd days after the initial injection. The haemoglobin level changed comparatively little even when no transfusions were given. The platelet count fell to under 100,000 per c.mm. in 8 patients, while the marrow in the area of distribution of the artery employed always became aplastic. Parasympathicomimetic reactions were observed in all 5 cases in which the internal or external carotid artery was used. These reactions consisted in meiosis, lacrimation, and salivation. In these cases also some radiomimetic changes, in the form of erythema, epilation, and inflammation of the epidermis or mucous membranes, were observed.

Subjective improvement was noted in 7 patients. In 6 the tumour decreased in size, while in 2 with intracranial lesions there was a fall in the intracranial pressure. Histological evidence of regression was found in 5 out of 9 cases where specimens were available. Of the total of 14 patients 12 died between 4 days and 6 months after the start of treatment; one patient was alive 4 months afterwards but there was slow progression of the disease. One patient with rhabdomyosarcoma of the thigh responded well; intra-arterial nitrogen-mustard therapy was followed by amputation, and the patient was alive without evidence of recurrence 14 months after the initial treatment. *H. F. Reichenfeld*

346. **Comparative Merits of 3:4-Dimethyl-5-sulfanilamido-isoxazole (Gantrisin) and a Sulfapyrimidine Triple Mixture**
D. LEHR. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **3**, 71–93, Jan., 1953. 4 figs., 44 refs.

At the New York Medical College the absorption, blood levels, and excretion of a 5% solution of " gantrisin " (sulphafurazole) were compared with those of a triple mixture of equal parts of 5% solutions of the sodium salts of sulphadiazine, sulphamerazine, and sulphamethazine on administration to rats, rabbits, and human subjects by various routes.

Both preparations were equally well absorbed when given by mouth, but gantrisin was much more rapidly excreted by the kidney. It is, however, poorly soluble in urine of *p*H less than 5·5, and the same is true of its acetyl derivative. Its diffusion through the blood–brain barrier was found to be much less than that of the triple mixture. The antibacterial potency *in vitro* was approximately the same for both preparations for a large number of organisms examined. *V. J. Woolley*

347. **The Relative Activity of the Common Sulfonamides against Experimental Toxoplasmosis in the Mouse**
D. E. EYLES and N. COLEMAN. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] 2, 54–63, Jan., 1953. 15 refs.

ANTIBIOTICS

348. **The Fixation of Streptomycin in the Pulmonary Alveoli after Intratracheal Administration.** (Sur la fixation de la streptomycine introduite par voie endotrachéale au niveau des alvéoles pulmonaires)
C. GRASSI. *Acta tuberculosea Scandinavica* [*Acta tuberc. scand.*] **27**, 207–210, 1952. 6 refs.

Unlike other positively charged molecules, streptomycin is fixed selectively in pulmonary tissue after endotracheal injection. This occurs irrespective of the *p*H or the volume of solution injected. In this investigation, carried out at the Institute of Bacteriology, University of Oslo, 10 rabbits examined 1 to 48 hours after endotracheal injection showed higher concentrations of streptomycin in lung tissue (1,500 μg. declining to 800 μg. per g. of tissue) up to 6 hours after injection than in the bloodstream (35 to 3 μg. per ml. of serum). In contrast, in 4 rabbits given endotracheal penicillin the blood concentrations (60 units per ml. after 1 hour and 20 units per ml. after 2 hours) were higher than those in pulmonary tissue (50 units per g. of tissue after 1 hour, and 5 units after 2 hours).

This fixation of streptomycin in pulmonary tissue is not considered to be due to any " organ tropism ", since the concentration attained in the lung after intravenous or intramuscular injection is low, and less than the blood level. The same is true of other organs.

It was shown that aureomycin and chloramphenicol behave in the same way as penicillin; terramycin, on the other hand, behaves like streptomycin but not so much is retained in the lung. *D. Weitzman*

349. **Investigation of Mechanism and Type of Jaundice Produced by Large Doses of Parenterally Administered Aureomycin**
J. C. BATEMAN, J. R. BARBERIO, J. K. CROMER, and C. T. KLOPP. *Antiobiotics and Chemotherapy* [*Antibiot. and Chemother.*] **3**, 1–15, Jan., 1953. 10 figs., 29 refs.

At the George Washington University Cancer Clinic, Washington, D.C., 24 patients with inoperable carcinoma received 26 courses of treatment with aureomycin introduced intra-arterially direct to the tumour site. Several of them were also treated with nitrogen mustard or *x* rays, but these caused no significant change in the results observed. The total dose of aureomycin was 4·5 to 64 g. given over 4 to 61 days in doses of 2 g. per day.

Determinations were made of the prothrombin time, cephalin flocculation, bromsulphalein retention, thymol turbidity, serum bilirubin level, icterus index, and serum non-protein nitrogen content. The only important changes were an increase in bromsulphalein retention and in serum bilirubin and non-protein nitrogen values, and these returned to normal when aureomycin was discontinued. The changes were presumably due to an intrahepatic obstructive jaundice, but bile pigment did not disappear from the stools. The icterus index and non-protein nitrogen values are considered to be the most useful signs of aureomycin overdosage.
V. J. Woolley

350. **Magnamycin. II. *In vivo* Studies**
A. R. ENGLISH, H. E. MULLADY, and R. A. FITTS. *Antibotics and Chemotherapy* [*Antibiot. and Chemother.*] **3**, 94–98, Jan., 1953. 4 refs.

"Magnamycin" (carbomycin), a crystalline preparation from *Streptomyces halstedii*, has been shown (*Antibiot. and Chemother.*, 1952, **2**, 678; *Abstracts of World Medicine*, 1953, **13**, 453) to have high activity *in vitro* against many Gram-positive organisms. Its ability to protect mice against infection by *Streptococcus pyogenes*, *Diplococcus pneumoniae*, and *Micrococcus pyogenes* var. *aureus* is now reported. The infections were produced by intraperitoneal injection, and the antibiotic was given either subcutaneously or intraperitoneally. Against the first two organisms magnamycin was less active than penicillin, but against *M. pyogenes* a dose of 40 mg. per kg. body weight was completely protective, while 80 mg. per kg. of penicillin was ineffective. *V. J. Woolley*

351. **N:N′-Dibenzylethylenediamine Penicillin: a New Repository Form of Penicillin**
A. P. FLETCHER and C. R. KNAPPETT. *British Medical Journal* [*Brit. med. J.*] **1**, 188–189, Jan. 24, 1953. 7 refs.

A new form of penicillin, N:N′-dibenzylethylenediamine (" benzethacil "), the properties and preparation of which have already been described (*Antibiot. and Chemother.*, 1951, **1**, 491; *Abstracts of World Medicine*, 1952, **12**, 13), was used in an investigation at St. Mary's Hospital, London, of the serum penicillin level after intramuscular injection of the drug. A single intramuscular injection of 1 ml. of an aqueous suspension containing 600,000 units of penicillin was given to 19 male volunteers whose ages ranged from 19 to 33 years. It was found that benzethacil administered by this route gave a sustained serum level of penicillin which was considerably higher than that obtained with any repository preparation of penicillin yet developed. In a few instances penicillin could be detected in the serum 28 days after a single intramuscular injection. The authors suggest that a summation of dose effect may occur even if the injections are spaced as far apart as 14 days. They point out that in some subjects an assayable level of penicillin was observed only intermittently, a phenomenon which may provide optimum conditions for the emergence of drug-resistant strains; moreover the incidence of sensitization to this preparation is not yet known. Further clinical study will therefore be required before the dangers of drug resistance and sensitization can be fully assessed. *A. W. H. Foxell*

352. **Practical Penicillin**
R. I. COHEN. *Lancet* [*Lancet*] **1**, 168–170, Jan. 24, 1953. 2 figs., 4 refs.

Although a daily dose of 300,000 units of an aqueous suspension of penicillin provides a bacteriostatic level in the blood for 24 hours, a single dose of 1·5 mega units of procaine penicillin will yield an adequate blood level of penicillin for 3 or 4 days. In 191 out of a series of 200 consecutive cases of infection of various types seen at a Liverpool hospital, the infection subsided in 7 to 10 days after a single massive injection of penicillin. It is suggested that such a dose lowers the vitality of organisms and gives time for the patient's own resistance to become established and so overcome any remaining infection.

To test the value of this method of treatment in general practice a single injection of 1·5 mega units of procaine penicillin was given to 135 patients attending a surgery in one of the poorest districts of Liverpool. The infection subsided in all except 2 cases in which an abscess formed, requiring incision. It is concluded that treatment of infections with a single massive dose of penicillin will lighten the work of the general practitioner and reduce the number of patients who attend the casualty departments of hospitals. Moreover, a nervous child will be spared the repeated injections which are necessary when aqueous solutions of crystalline (soluble) penicillin are given.

Convincing charts and tables showing the results of treatment are presented. [This article is one of practical importance, and the conclusions are based on a careful survey of an adequate number of cases. The contention of the author that a single massive dose of procaine penicillin is time-saving for all concerned, including the patient, appears to be fully justified, and it is to be hoped that the advantages of this procedure will be speedily recognized.] *R. J. MacNeill Love*

353. **On the Duration of Penicillin Action in Relation to Its Concentration in the Serum**
H. EAGLE, R. FLEISCHMAN, and M. LEVY. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **41**, 122–132, Jan., 1953. 2 figs., 12 refs.

The therapeutic effect of penicillin has been regarded as largely due to the aggregate time it remains at effective levels at the focus of infection, these levels being of the same order *in vivo* as *in vitro*, and the effective time in the serum approximately equal to that in the tissue fluids. Other work, however, has suggested that the bactericidal action of penicillin regularly and significantly persists after it is no longer demonstrable in the blood, either by its persistence in the tissue fluid or by its so affecting the bacteria that they can be disposed of by host defence-processes after the antibiotic has become ineffective.

The authors, working in the Section of Experimental Therapeutics of the U.S. National Institutes of Health, Bethesda, have attempted to resolve these views. They found no evidence of persistence of the drug at effective levels in normal skin, muscle, testis, or peritoneal cavity of mice or rabbits. Direct measurement of bactericidal action in terms of serum concentration was determined by the intramuscular injection into the hind leg of 20-g. mice of 4×10^6 organisms (Group-A streptococci) in 0·15 ml. of fluid and by giving 2 hours later 0·15 ml. of aqueous sodium benzyl penicillin containing doses of 0·05, 0·20, 0·80, 3·2, 12·5, or 50 mg. per kg. body weight intramuscularly in the opposite leg. After varying time intervals groups of 8 to 12 mice were killed, the inoculated muscle aseptically emulsified in 50 ml. of 1% blood broth, and the number of viable organisms determined by plate counts. The results were related to the times at which

the serum penicillin concentration exceeded 0·05 μg. per ml. and fell below 0·02 μg. per ml., the maximum and minimum effective concentrations. They showed that: (1) the initial rate of kill of organisms was independent of dosage and of magnitude of serum concentration, provided this was above the maximum; (2) that the importance of dosage was in relation to duration of bactericidal action; (3) the duration of the period of bacterial recovery varied widely, being brief after small doses but lasting 4 to 6 hours after 3·2 to 50 mg. per kg. body weight, and that in this period host defences were of little effect; (4) when the organisms had recovered, multiplication was resumed and the mice eventually succumbed to septicaemia.

In further experiments the duration of protection given by a single large dose of 60 mg. of sodium penicillin per kg. body weight when followed by the injection of 200 organisms (Group-A streptococci or Type-III pneumococci) intramuscularly, intraperitoneally, or subcutaneously, was determined in mice, and also in rabbits which were given an intratesticular injection of Group-B haemolytic streptococci (*Str. agalactiae*). It was then shown that half of these animals succumbed to the challenge inoculum when this was given 1·3, 1·6, or 2·6 hours after the penicillin, that is, 1·4, 1·1, or 0·1 hours before the serum penicillin level had fallen to 0·05 μg. per ml.

There was no indication, therefore, in these experiments that penicillin persisted at effective levels in the tissue fluids of normal animals for significantly longer periods than in the serum. Previous anomalous results might be accounted for by the use of repository penicillin preparations. In general, the only advantage of large doses is the longer effective period. The authors consider that host defence-mechanisms do little to enhance the bactericidal action of penicillin and conclude " that in the nonimmune animal the primary determinant of the therapeutic activity of penicillin is the total time for which it remains at the focus of infection in concentrations effective against the particular organism ".

Malcolm Woodbine

354. **Penicillin Anaphylaxis**

P. S. MAYER, M. M. MOSKO, P. J. SCHUTZ, F. A. OSTERMAN, L. H. STEEN, and L. A. BAKER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 351–353, Jan. 31, 1953.

355. **Action of Antibiotics on Avian Tubercle Bacilli Studied with the Electron Microscope**

E. M. BRIEGER, V. E. COSSLETT, and A. M. GLAUERT. *Nature* [*Nature* (*Lond.*)] **171**, 211–212, Jan. 31, 1953. 4 figs., 1 ref.

The authors, working at the Papworth Hospital and the Strangeways and Cavendish Laboratories, Cambridge, have devised special techniques for growing tubercle bacilli on stainless-steel electron-microscope grids using liquid media. The method has been used to study the effect of streptomycin and isoniazid in concentrations of 10, 20, and 100 μg. per ml. of Dubos medium. The bacilli retained their acid-fastness after exposure to the electron beam. In normal conditions the short bipolar rods elongated up to 7 times their original length in 24 hours but broke down to individual rods after 3 days. In the presence of streptomycin, cultures grew more slowly and formed broader filaments with an indefinite internal structure. Any mycelial tendencies were encouraged by small doses of streptomycin; higher concentrations of the antibiotic arrested growth at the mycelial stage. On the other hand, isoniazid in a concentration of 10 μg. per ml. had little visible effect on growth patterns. At 20 μg. per ml., however, the rods shrivelled, lost their transparency, and appeared as dense oval bodies. After 3 days normal filaments then developed by the side of the tapering rods, and after 7 days the cultures partially recovered, to give a mass of filaments. At higher concentrations (100 μg. per ml.) recovery was later and growth much retarded.

Thus streptomycin and isoniazid attack the tubercle bacillus in different ways. The initial inhibition by isoniazid and the delayed action of streptomycin suggest, as has been recognized clinically, that a combination of the two should give promising results. This technique, therefore, is of value in assessing antibiotic action at a very early stage. The observations, it is pointed out, were made on an avian strain of tubercle bacilli which had lost much of its virulence. *Malcolm Woodbine*

356. **Clinical Aspects of the Toxicity of Polymyxins A, B, and E**

P. N. SWIFT and S. R. M. BUSHBY. *Lancet* [*Lancet*] **1**, 110–112, Jan. 17, 1953. 16 refs.

The polymyxins, which are polypeptide antibiotics derived from different strains of *Bacillus polymyxa*, have not become popular, perhaps because of their tendency to cause proteinuria. In previous trials at Farnborough Hospital, Kent, polymyxin A in doses of 4,000 to 10,000 units per kg. body weight 4-hourly intramuscularly for 5 days produced proteinuria ranging from a trace to 0·2 g. per litre in 26 out of 27 children. There were no reactions at the injection site.

In more recent trials here reported no proteinuria was seen in 53 patients receiving polymyxin E or in 32 receiving polymyxin B parenterally in 4-hourly doses of 10,000 to 12,500 units per kg. body weight for children, and 250,000 units per kg. body weight for adults. Troublesome reactions—especially mild pain at the site of injection—for some hours were observed with polymyxin B, and some patients developed slight pyrexia, malaise, and mild paraesthesiae. These reactions were less frequent with purer preparations. Polymyxin E was less painful at the injection site than polymyxin B, but the incidence of paraesthesiae was about the same, and 2 patients developed urticaria. Polymyxins given by mouth or locally for burns were poorly absorbed and produced no toxic or side-effects. The authors suggest that the various side-effects of different polymyxins are due to differences in the molecular structure, and that some symptoms are due to the release of endogenous histamine. The side-effects produced by parenteral polymyxins B and E were not considered severe enough to contraindicate their use in therapy. *I. Ansell*

Infectious Diseases

VIRUS INFECTIONS

357. **The Radiological Changes in the Lungs in Children with Measles in Relation to the Clinical Picture.** (Die Veränderungen der kindlichen Lunge bei Masern im Röntgenbild unter Berücksichtigung der Klinik)
E. HAUSMANN and R. SEYSS. *Österreichische Zeitschrift für Kinderheilkunde und Kinderfürsorge* [*Öst. Z. Kinderheilk.*] **8**, 206–218, 1953. 5 figs., 18 refs.

During the latter part of 1950 and the early months of 1951 the authors noted an increase in the number of cases of measles and whooping-cough (while those of scarlet fever and diphtheria decreased) admitted to the Wilhelmina Hospital, Vienna. In several respects the two diseases showed clinical and pathological similarities.

In this paper the authors relate the radiological changes in the lungs to the clinical picture as seen in children with measles. Although some children were examined during the incubation period, no significant radiological changes were observed at this stage. With the onset of the rash and the accompanying bronchitis, however, radiological changes began. There were both thickening and enlargement of the hilar shadow, and coarse striations were seen basally running far into the periphery. In 56 of the 150 cases there were no further changes, and the radiological picture returned to normal as the disease abated.

In more severe forms of the infection, however, a condition was seen which was difficult to fit into the category of either bronchiolitis or bronchopneumonia; the authors labelled it broncho-bronchiolitis. Clinically there were slight cyanosis, dyspnoea, and moist sounds throughout the lungs, but hyperresonance rather than dullness on percussion. The changes in the *x*-ray picture were primarily in the bronchial tree. The hilar and central areas produced a homogeneous shadow, due to the inflammation of closely approximated bronchi and bronchioles. The increase in the peripheral shadows which was present was not due solely to congestion, since an abrupt alteration in the bronchial lumen could be seen. Between these coarse striations were finer linear shadows, so that in spite of an apparently uniform appearance no single picture resembled another. The authors refer to this type of picture as showing centrobasal shadows. Further development of this stage was variable. In some cases the child improved over-night, although no sudden change occurred in the radiological picture; in other cases there was a worsening of the condition and development of a bronchiolitis with marked clinical signs, and here the radiograph showed either increased linear markings or a miliary mottling, with or without confluence. A third type of case showed a true bronchopneumonia with characteristic changes. Lobar pneumonia occurred twice, in both cases as a sequel to the measles. Atelectasis, either occurring as middle-lobe collapse or in small scattered patches, was also observed. The authors found that there was a greater incidence of severe lung changes in children in a poor nutritional state, or in those who had had previous chest trouble or in whom the initial stages of the measles were severe. *J. G. Jamieson*

358. **Comparative Study of Canine Distemper and a Respiratory Disease of Man**
J. M. ADAMS. *Pediatrics* [*Pediatrics*] **11**, 15–27, Jan., 1953. 8 figs., 16 refs.

In this paper from the University of California, Los Angeles, evidence from the literature is cited supporting the view that the virus of canine distemper is infective for man. A series of photomicrographs shows the resemblance between inclusion bodies found in human pharyngeal, broncho-pulmonary, and bladder epithelium and those found in the same tissues in dogs and ferrets with distemper, and histological similarities are also pointed out [in most of the examples the disease, if any, from which the human beings were suffering is not made clear]. In a series of experiments carried out on ferrets, of which details are given, human gamma globulin proved as effective as hyperimmune distemper antiserum in neutralizing distemper virus *in vitro* or modifying the illness produced by its injection. The development of neutralizing antibodies to a chick-embryo-adapted strain of distemper virus was demonstrated in 2 children with an acute respiratory infection.

[These observations suggest that canine distemper virus sometimes infects man and may conceivably cause respiratory symptoms. Whether they justify the author's assertion of its possible relationship to the epidemic respiratory disease of infants previously described by him (*Proc. Soc. exp. Biol.* (*N.Y.*), 1941, **46**, 114) is open to question.] *H. McC. Giles*

359. **Meteorological Conditions in Relation to Poliomyelitis in England and Wales 1947–1952**
W. H. BRADLEY and A. E. RICHMOND. *Monthly Bulletin of the Ministry of Health* [*Monthly Bull. Minist. Hlth* (*Lond.*)] **12**, 2–15, Jan., 1953. 8 figs.

The authors report a statistical investigation, carried out at the Ministry of Health, London, to discover whether meterorological conditions could be related to the well-known seasonal variation in the incidence of poliomyelitis. The investigation was directed towards determining: (1) whether there were thresholds of temperature and humidity which governed the seasonal rise; (2) whether there were similar thresholds dictating the seasonal fall; (3) if weekly variations in meteorological conditions during the poliomyelitis season influenced the incidence at the corresponding time; and (4) if the total meteorological constitution during the poliomyelitis season in each year governed or influenced

the incidence of disease in that season. Temperature and humidity, which are stated in terms of dry-bulb (DB) temperature and vapour pressure (VP), were studied in relation to notifications (uncorrected) of poliomyelitis in several counties in England and Wales from 1947 to 1952. (Full statistical tables and charts are provided.) The authors' conclusions are entirely negative. They state, however, that in the short period of 6 years there was a tendency for the incidence of poliomyelitis to be lowest in seasons with a low average DB–VP reading, but they admit that this could have occurred by chance.

It would appear that the study of meteorological conditions is not likely to prove of help in predicting the incidence of poliomyelitis. *Joseph Ellison*

360. **Orthopedic Treatment of Acute and Subacute Poliomyelitis by Early Stretching with the Aid of Curare**
V. H. RAISMAN and J. SCHNEIDERMAN. *Journal of the International College of Surgeons* [*J. int. Coll. Surg.*] **19**, 93–103, Jan., 1953. 2 figs., 20 refs.

BACTERIAL INFECTIONS

361. **Diagnostic and Therapeutic Clues in the Study of Tetanus**
R. P. SCHMIDT, L. L. LEVY, R. C. TURRELL, W. E. HOPKINS, B. M. BLOOR, and E. ROSEMAN. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. (Chicago)*] **69**, 55–63, Jan., 1953. 3 figs., 18 refs.

An account is presented of the treatment given, and of simultaneous electroencephalographic and electromyographic studies carried out, at the Louisville General Hospital in 13 cases of tetanus. Untreated patients showed no appreciable alterations in the electroencephalogram (EEG) even during spasms. Delta activity appeared only terminally or when the patient was under the influence of sedatives. All the patients were treated with tetanus antitoxin and penicillin, and in 6 cases sedatives, in heavy doses, were given in addition; in none of these could the spontaneous or induced tetanic myographic responses be abolished. Five patients were given tubocurarine intravenously in small doses at frequent intervals to a point where spontaneous and induced tetanic seizures disappeared clinically and electromyographically for 40 to 60 minutes or more without serious disturbance of the respiratory exchange or alteration in the EEG. The last 2 of these were successfully maintained free of spasms for periods of 10 and 14 days respectively by the regular periodic administration of tubocurarine with only enough sedation to allay anxiety and secure adequate rest. The maintenance dose of tubocurarine varied from 10 to 20 units and was given intravenously every hour as long as the patient continued to show any evidence of spontaneous or induced tetanic seizures. The other 3 patients were given tubocurarine for an unspecified period, being subsequently treated by the usual sedative technique. A team was organized in association with the anaesthetic department to ensure the maintenance of an adequate airway during tubocurarine therapy and to provide artificial respiration if necessary. The technique used for determining the dosage required is described.

[It is not specifically stated how many of these 13 patients died, and 2 patients are not accounted for in the figures given above. It is, however, stated that the 2 receiving prolonged tubocurarine therapy survived. Although the diagnosis of tetanus is not always easy, the statement in this paper that the "combination of unaltered brain waves and the typical myographic response during a convulsion would seem to point to a diagnosis of tetanus" would shock most British clinicians.]
J. MacD. Holmes

362. **Oxytetracycline–Streptomyin Therapy in Brucellosis due to *Brucella melitensis***
G. B. MAGILL and J. H. KILLOUGH. *Archives of Internal Medicine* [*Arch. intern. Med.*] **91**, 204–211, Feb., 1953. 2 figs., 16 refs.

363. **Chronic Brucellosis**
G. M. BARRETT and A. G. RICKARDS. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **22**, 23–42, Jan., 1953. 6 figs., bibliography.

Chronic brucellosis has not been much studied in Great Britain and little is known of its incidence. With the extension of consultant services to the rural areas under the National Health Service and the increasing awareness of the occurrence of this disease it is to be expected that many more cases will be brought to light. [This article should be of great assistance in this respect: it is one of the most informative which the abstracter has read on the subject, especially in respect of diagnosis.]

The authors, working at the Royal Lancaster Infirmary, have access to a rural district in which only 1% to 15% of the milk consumed is heat-treated. They describe 25 cases of chronic brucellosis in patients varying in age from 21 to 68 years, the majority being farmers and others who are in frequent contact with cattle, these forming part of a series of 62 cases diagnosed in the area within a period of 18 months. Males greatly predominated and twice as many of the patients were over as were under 40 years of age. One patient exhibited in addition all the diagnostic features of infectious mononucleosis.

The chief criteria for the diagnosis of chronic brucellosis are: (1) a long-standing history of night sweats and diffuse or localized muscle pain (usually described as "rheumatism") in a patient who has not lost weight and does not look ill; (2) a history of contact with cattle; (3) enlargement of the liver or spleen or both, occasionally with lymphadenopathy; (4) relatively normal erythrocyte sedimentation rate and blood count; (5) positive serum agglutination of *Brucella* and positive skin reaction to brucellin; (6) if serum agglutination is negative but the skin reaction positive, markedly positive agglutination 2 weeks later is very suggestive of chronic brucellosis provided that the history and clinical findings are also suggestive; (7) if, in such a case, the second agglutination test shows only a small rise in titre, liver biopsy is justified, the biopsy in cases of the disease showing nodular granulomata resembling non-caseating miliary

tubercles and not related to the portal tracts or specific zones of the liver lobule. In 10 out of 12 cases in the present series in which liver biopsy was performed these nodular granulomata were found, and in view of the fact that they are indistinguishable from sarcoid lesions it is suggested that chronic brucellosis may be one form of sarcoidosis.

[It is unfortunate that treatment is not dealt with fully in this excellent paper, but indications are given of occasional success with aureomycin, sometimes combined with intravenous injections of typhoid–paratyphoid vaccine.] *H. Stanley Banks*

LOCAL INFECTIONS

364. **Hemolytic Streptococcus Gangrene. A Report of Seven Cases**

W. L. WHITE. *Plastic and Reconstructive Surgery* [*Plast. reconstr. Surg.*] **11**, 1–14, Jan., 1953. 5 figs., 13 refs.

The chief feature of haemolytic streptococcal gangrene is a primary infective necrosis of the deep fascia, which spreads widely, with secondary gangrene of the overlying skin and subcutaneous tissue. The author describes 7 cases seen in hospital in Pittsburgh, of which 6 were in patients over the age of 50. Onset is usually associated with superficial or penetrating injury, but this may be trivial or even apparently absent. The clinical course is typically fulminating and associated with great physical prostration and a curious mental state of indifference. Diagnosis is usually made on the appearance of skin gangrene, and unless the area is incised early down to the necrotic fascia, the causal organism, a β-haemolytic streptococcus, is difficult to isolate, as secondary and saprophytic infections rapidly supervene. The author suggests that a factor specifically affecting collagenous fascial tissue is present. Widespread incision and excision of necrotic fascia are necessary in all cases, just as they were before the advent of antibiotics, so that considerable loss of tissue is likely and a subsequent skin graft necessary. *R. Weeden Butler*

365. **Infections of the Hand. A Review Based on 1,000 Consecutive Cases**

R. H. C. ROBINS. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **34B**, 567–580, Nov., 1952. 6 figs., 14 refs.

The two main problems in the management of infections of the hand are: (1) to restore the patient with a simple infection to full working capacity in the minimum time; and (2) to devise the best treatment for difficult and complicated conditions such as infections involving bones, joints, and tendon sheaths and extensive sloughing of skin and subcutaneous tissues. In approximately two-thirds of 1,000 consecutive cases treated at the Hand Clinic of the Royal Victoria Hospital, Newcastle-upon-Tyne, the patient gave a history of injury, the average time elapsing between injury and onset of infection being 4 days. It is noted that mining hazards accounted for 35% of all serious injuries, but for only 13% of the infections. The most common types of infection treated were subcutaneous infection (412 cases), infection of the pulp space (244), and infection around the nail (233). Other types treated were subcuticular infections, carbuncles, cellulitis, infections of the joints and deep palmar space, and primary infections of tendon sheaths. The most frequent serious complications were bone infection accompanying abscess of the pulp space, and widespread necrosis of the skin and subcutaneous tissue following subcutaneous infections.

The treatment generally adopted for simple infections in this series was by early drainage of pus under general anaesthesia (using a bloodless field), rest, and injections of 100,000 units of penicillin in aqueous solution every 6 hours, usually for 6 days. Dry dressings, changed frequently, were used postoperatively. Skin loss was usually slight and healing rapid, but skin grafting was used if there remained a granulating area of any extent; in most cases a Thiersch graft sufficed, but if digital nerves or tendons were exposed a full-thickness graft was used.

The author has found no satisfactory treatment for established bone infections, but considers that early recognition of the condition should enable the progress of the infection to be arrested.

(The article contains a detailed and valuable statistical analysis, and is illustrated in colour.)

Harold C. Edwards

366. **Results of Treatment of Infections of the Hand**

J. C. SCOTT and B. V. JONES. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **34B**, 581–587, Nov., 1952. 1 ref.

This article is, in effect, an extension of the preliminary report by Loudon *et al.* (*J. Bone Jt Surg.*, 1948, **30B**, 409; *Abstracts of World Surgery*, 1949, **5**, 91) on the method of treatment of infections of the hand adopted by the Accident Service of the United Oxford Hospitals. This consists in the excision of all devitalized tissue with immediate suture, plaster protection and immobilization, and parenteral penicillin. The authors now review the records of 1,211 patients treated for hand infections between July, 1948, and April, 1951, of whom 1,066 required operation. The results of treatment by this means of various types of infection are given. For example, of 347 cases of palmar infection of the finger 56% were healed in an average period of 11 days. In the 44% that failed to heal *per primum* the average delay in healing was 33 days. There was bone involvement in 20 cases, with sequestrum formation in 5.

The authors emphasize that treatment by excision should be used only when the infection is localized and where pus can be removed, dead tissue excised, and healthy skin sutured without tension. Its use is clearly indicated in tendon-sheath infections in which simple drainage gives such unsatisfactory results, and is superior to other forms of treatment for palmar infections with multilocular abscess. On the other hand, the method is contraindicated when infection is poorly localized or so extensive that excision is impracticable, and is unnecessary in trivial infections. *Harold C. Edwards*

Tuberculosis

367. **Tuberculosis in Young Children**
R. M. CAMMOCK and F. J. W. MILLER. *Lancet* [*Lancet*] **1**, 158–160, Jan. 24, 1953. 10 refs.

The morbidity from primary tuberculosis has been studied by the authors in a population of about 25,000 children, consisting of all children born in Newcastle upon Tyne between Jan. 1, 1945, and Dec. 31, 1949—that is, the population aged less than 5 years on the latter date. In a clinical survey (carried out independently by the City Health Department) of a representative sample of the infant population of the city nearly 1,000 families with infants born in May and June, 1947, were observed over a 5-year period, routine tuberculin testing being performed with old tuberculin jelly, followed in doubtful cases by an intradermal test with 10 units of old tuberculin. From the conversion rate so determined it was estimated that 1,020 (4%) of the 25,000 children had acquired a primary infection. By a careful and detailed search of the records in hospitals, chest clinics, and contact clinics serving the area up to the end of December, 1951, 258 of the estimated 1,020 children were traced, consisting of 98 notified cases, 21 hospital cases not notified, 134 household contacts attending observation clinics, and 5 other out-patients. Within a minimum period of 2 years after infection, 16 (1·5%) of the 1,020 had developed lesions of bone and 42 (4·1%) had developed either tuberculous meningitis or miliary tuberculosis, while 36 (3·5%) had died of tuberculosis. The risk of an infected child developing miliary tuberculosis or meningitis was calculated to be 1 in 20 at ages below 2 years and 1 in 30 at ages above 2 years.

J. G. Millichap

368. **Studies on the Concentration of Streptomycin in the Treatment of Bone and Joint Tuberculosis.** [In English]
M. FELLANDER, T. HIERTONN, and G. WALLMARK. *Acta tuberculosea Scandinavica* [*Acta tuberc. scand.*] **27**, 176–189, 1952. 15 figs., 16 refs.

At St. Göran's Hospital, Stockholm, in an attempt to determine the best method of administering streptomycin in the treatment of tuberculosis of bones and joints, the concentration of streptomycin in exudates, blood, and urine was determined in 25 cases of bone and joint tuberculosis after parenteral administration of the drug. In the osseous cases, the pus was obtained at operation. The streptomycin content was measured as described by Wallmark (*Acta. path. microbiol. scand.*, 1951, **29**, 397).

In 22 cases of osteitis, pus samples were examined 2 to 6 hours after the intramuscular injection of 0·5 g. of streptomycin. In 14 of these, bacteriostatic concentrations (1·1 to 18 μg. per ml., average 5·1 μg.) were found; in 3 cases there were traces only, and in 5 cases no streptomycin could be detected. These differences could not be accounted for on clinical or pathological grounds. Since the concentration reached is thus not always satisfactory, the authors advise that open operation and the local application of streptomycin powder should always be carried out in addition to parenteral administration of the antibiotic.

In 3 cases of tuberculous synovitis, bacteriostatic concentrations were found in joint fluid (obtained by needle puncture) up to 10 hours after intramuscular injection of 0·5 g. of streptomycin. It is therefore concluded that intramuscular therapy is effective in this type of case.

D. Weitzman

369. **Geographic Variation in Naturally Acquired Tuberculin Sensitivity**
L. B. EDWARDS and C. E. PALMER. *Lancet* [*Lancet*] **1**, 53–57, Jan. 10, 1953. 4 figs., 2 refs.

In this paper from the Tuberculosis Research Office of the World Health Organization, Copenhagen, an analysis is made of the differences in tuberculin sensitivity revealed by the results of Mantoux tests carried out on 9,845 children in Denmark, 1,737 in Mexico, 3,049 in Egypt, and 2,561 in South India. In India the initial test was made with a dose of 5 tuberculin units (T.U.) and in other countries with 10 T.U., 100 T.U. being used in all countries for the final test, which was carried out only when the area of induration after the initial test was less than 6 mm. in diameter. The children concerned had not been vaccinated with B.C.G., and were generally aged between 7 and 14 years. The frequency distribution of the various degrees of severity of reaction (as shown by the diameter of the area of induration) in each group is shown diagrammatically for both initial and final tests, and from an analysis of these diagrams it is concluded that in each country there is one group of children with high-grade tuberculin sensitivity, giving a strong reaction to the small dose, and another group with low-grade sensitivity, giving a minimal or no reaction to the smaller dose but a definite reaction to the larger dose, while a third group show little or no reaction to either the small or large dose of tuberculin and may be regarded as insensitive.

In Denmark and India a relatively small percentage of children show high-grade sensitivity, which occurs more frequently in Mexico and Egypt. Low-grade sensitivity is practically absent in Denmark and Mexico, fairly prevalent in India, and much more frequent in Egypt. This lack of correlation in distribution between high-grade and low-grade sensitivity is regarded by the authors as presumptive evidence that the two types do not have the same cause; it is suggested that high-grade sensitivity represents a specific reaction to tuberculous infection, while low-grade sensitivity is independent of infection, but closely associated with geographical factors.

T. M. Pollock

RESPIRATORY TUBERCULOSIS

370. Serial Haemagglutination Tests during the Treatment of Pulmonary Tuberculosis

D. A. L. Bowen and R. C. Jennings. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **47**, 41–45, Jan., 1953. 8 refs.

It is now known that the Middlebrook and Dubos haemagglutination tests for the detection of antibodies against the tubercle bacillus is of little use in the diagnosis and prognosis of pulmonary tuberculosis; positive reactions have been found in non-tuberculous controls and negative reactions may be obtained in tuberculous patients. However, the test is still of some value in the differential diagnosis of obscure shadows in radiographs of the chest.

As most previous workers had relied on single readings of the haemagglutination titre the authors, in the hope that serial readings might prove a more reliable prognostic aid, made serial examinations of the serum of 111 patients at the London Chest Hospital over periods of 3 to 14 months. The patients were divided into four groups: (1) 25 patients undergoing resection; (2) 26 patients on whom thoracoplasty was performed; (3) 28 cases treated medically; and (4) 32 patients treated with isoniazid. In all groups the serum was examined before and for several months after treatment.

The haemagglutination titre showed no change in 21 out of the 25 cases undergoing resection, in 23 of the 26 cases undergoing thoracoplasty, in 29 out of the 32 cases treated with isoniazid alone, and also no change in 20 out of the 28 patients having other forms of medical treatment.

The authors suggest that once the antibodies reach a certain level their pattern stays constant, even though the tuberculous lesion has become stabilized, is healing, or has been excised. It is therefore concluded that serial haemagglutination tests are of no value in the prognosis of pulmonary tuberculosis. *T. Marmion*

371. Bronchial Obstruction and Bronchiectasis Complicating Primary Tuberculous Infection

J. B. Hardy, D. F. Proctor, and J. A. Turner. *Journal of Pediatrics* [*J. Pediat.*] **41**, 740–755, Dec., 1952. 8 figs. 22 refs.

Bronchiectasis is a well-known complication of acute respiratory infections, but only during the last 20 years has it been recognized as a sequel of primary tuberculosis. The nature and anatomical pattern of spread of the primary disease give rise to a bronchiectasis which has a different distribution from that seen in cases of reinfection tuberculosis, where the bronchiectatic lesions are in the diseased area. Bronchial obstruction and secondary infection are significant aetiological factors in the production of bronchial dilatation following primary tuberculosis. The bronchi may be obstructed by enlarged lymph nodes, by the rupture of a caseous node through the bronchial wall with resulting endobronchial disease, by caseous disease in the bronchus, or by stricture following a bronchial perforation.

The authors of the present paper report their findings in 35 cases in which there was evidence of bronchial obstruction following primary tuberculous infection. Bronchoscopy was carried out on 29 of the patients and revealed bronchial occlusion, due wholly or in part to endobronchial disease, in 10, evidence of acute non-specific infection in 5, and chronic secondary pyogenic infection in 11. In one case the occlusion was due to extrinsic pressure alone; the other patients had no signs of endobronchial disease. Bronchograms showed that there was an equal incidence of saccular and of tubular bronchiectasis. The authors recommend bronchoscopy for all patients with signs of bronchial obstruction, as aspiration and surgical removal of granulation tissue may be possible.

A study of the post-mortem findings in 186 children who died from tuberculosis revealed that 15 had bronchiectasis as a complication of primary tuberculous infection. It is held that this incidence of bronchial disease is low, and that had the condition been specifically looked for, a higher incidence would have been recorded.

T. Marmion

372. The Bronchus—the Clue to the Pathogenesis and Treatment of Pulmonary Tuberculosis

F. H. Young. *Edinburgh Medical Journal* [*Edinb. med. J.*] **60**, 77–94, Feb., 1953. 21 refs.

373. Extrapleural Pneumothorax

J. W. Streider and E. A. Gaensler. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **67**, 3–21, Jan., 1953. 7 figs., 24 refs.

Out of a total of 323 patients undergoing primary operations for the treatment of pulmonary tuberculosis in the Sanatorium Division of the Boston City Hospital between 1947 and 1951, extrapleural pneumonolysis was carried out on 47 (14·5%). The patients selected for this operation fell into two groups: (1) those with respiratory insufficiency due to advanced bilateral disease or previous contralateral surgery (32 cases); and (2) those with less severe disease, suitable for collapse therapy, where absence of deformity was particularly to be desired (15 cases). In the latter group extrapleural pneumothorax was at first always followed by modified thoracoplasty, but this has now been abandoned in favour of extraperiosteal plombage.

Minor complications occurred in 7 cases and major complications, leading to the abandonment of the pneumothorax, in 8. There was one case of tuberculous infection of the extrapleural space, but none of secondary infection. Operative mortality was *nil*, but there were 4 late deaths. Of the remaining 43 patients, 32 were discharged well 6 months to a year after the operation, but 19 of these later underwent thoracoplasty; in 9 patients the space could not be maintained after the primary operation and thoracoplasty or lobectomy was therefore performed without delay, all these patients being then discharged well; and 2 patients refused further treatment.

[The results in the two groups of cases are not stated separately.] *S. F. Stephenson*

374. **Intermediary Report of 102 Streptomycin-protected Pulmonary Resections**
J. D. MURPHY and B. B. BECKER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **67**, 22–28, Jan., 1953.

At the Veterans Administration Hospital, Oteen, North Carolina, 100 patients underwent pulmonary resection for tuberculosis between 1945 and 1948, lobectomy being performed in 49 cases and pneumonectomy in 51. In 41 cases the operation was performed because of failure of thoracoplasty. Streptomycin was given for one week before and 2 weeks after operation [dosage not stated], none of the patients having previously received the drug. There were 7 early and 2 late deaths. The complications included broncho-pleural fistula in 10 cases (in 9 of which it followed pneumonectomy) and late re-activation in 15 cases (in 3 of which it followed pneumonectomy). Late development of extrapulmonary tuberculosis occurred in 4 cases. After a follow-up period of at least 3 years, 9 patients were dead, 11 were in hospital, and 80 were well; the sputum was positive in 6, infrequently positive in 23, and negative in 62 of the surviving patients.

The authors suggest that these relatively good results are due partly to the fact that the patients were treated in the early days of resection, when cases were selected for the operation within narrower limits than are applied today, and partly to the high proportion of patients who, having already undergone thoracoplasty and survived without the benefit of chemotherapy, might be presumed to have a high degree of " inherent native resistance ".

S. F. Stephenson

375. **The Status of Closed Pneumonolysis (Jacobaeus). An Historical Review and an Analysis of One Hundred and Fourteen Cases**
L. GOLDBERG. *Quarterly Bulletin of Sea View Hospital* [*Quart. Bull. Sea View Hosp.*] **14**, 15–27, Jan., 1953. 9 refs.

376. ***para*-Aminosalicylic Acid (PAS) and Streptomycin in Pulmonary Tuberculosis. Comparison between 84 PAS-treated and 82 Streptomycin-treated Cases.** [In English]
THE SWEDISH NATIONAL ASSOCIATION AGAINST TUBERCULOSIS: THERAPEUTIC TRIALS COMMITTEE. *Acta tuberculosea Scandinavica* [*Acta tuberc. scand.*] **27**, 157–175, 1952. 8 figs., 23 refs.

A comparison of the results of treatment was made between 84 patients with pulmonary tuberculosis who were treated with 10 g. of PAS daily and 82 who were given 1 g. of streptomycin daily for 3 months (in 85% of the cases). The cases included both acute and chronic types of disease, with and without cavitation, the proportion of each being similar in the two series.

In both groups febrile cases showed a fall in temperature, PAS and streptomycin appearing to be equally effective in this respect. The erythrocyte sedimentation rate fell slightly (but significantly) more rapidly in the PAS-treated cases. Weight gain was more rapid in the streptomycin-treated group, especially in male patients. The rate of sputum conversion was similar in the two groups. Radiological improvement occurred in 71% of the streptomycin-treated cases and in 62% of those receiving PAS; the best results were seen in female patients treated with streptomycin. Side-effects caused treatment to be stopped in 3 cases receiving PAS and 8 being treated with streptomycin.

The authors point out that results with PAS were virtually as good as those with streptomycin. Since side-effects were less severe and drug-resistance slower to develop with PAS, they conclude that PAS is the drug of choice in cases requiring long-continued treatment, while in subchronic cases a combination of the two drugs may be worth trying.

D. Weitzman

377. **Technique, Results of and Indications for the Treatment of Pulmonary Tuberculosis by Short Intravenous Transfusion of PAS.** [In English]
G. FAVEZ, A. BOSSY, G. DITTRICH, E. EDDE, and A. LOCKHART. *Acta tuberculosea Scandinavia* [*Acta tuberc. scand.*] **27**, 190–206, 1952. 16 figs., bibliography.

In this paper the authors strongly advocate the administration of PAS for the treatment of pulmonary tuberculosis by short intravenous infusions; and by " short " they mean that the duration of each single infusion is not more than 1 to 1½ hours. At Mont Blanc Sanatorium, Leysin, Switzerland, the following scheme of treatment has given remarkable results: 18·5 g. of PAS in 500 ml. of water is given by intravenous infusion daily on 5 days each week for the first 4 weeks; the same regimen is then continued with the addition of 1 g. of streptomycin every 3rd day for 4 to 6 months. The best results are obtained from the use of freshly-prepared solutions of pure PAS (free from *m*-aminophenol) in pyrogen-free distilled water, sterilized in a current of steam and used as soon as possible after preparation.

This treatment is particularly indicated in recent cases, that is, those diagnosed in the previous 8 to 12 months, and it is most effective in cases with diffuse nodular lesions. The sputum rapidly becomes negative, while radiological improvement is most apparent during the first 8 to 12 infusions, slowing down later as the proportion of long-standing opacities increases. PAS infusion is also useful as a preliminary to collapse therapy, and if this is intended it should be planned before starting the course of infusions; improvement noted as a result of the infusions of PAS, unless it is very striking, should not alter any decision thus made.

In regard to side-effects, gastro-intestinal disturbance has been minimal, no evidence of renal or hepatic dysfunction has been seen, and allergic phenomena have been uncommon. In a few, exceptional, cases petechiae have appeared, but there were no serious haemorrhagic phenomena. In view, however, of the possible danger of hypoprothrombinaemia, vitamin K should be injected daily for 4 weeks before any surgical procedure, and PAS should be discontinued for two weeks from the day preceding operation. Four illustrative cases are described.

D. Weitzman

See also Chemotherapy, Abstract 348

Venereal Diseases

SYPHILIS

378. A Preliminary Study of Apparent Biological False Positive Reactions in Four Serological Tests for Syphilis, and the Treponemal Immobilization Test

S. OLANSKY, A. HARRIS, and J. H. HILL. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 23–28, Jan., 1953. 16 refs.

The authors, from the Venereal Disease Research Laboratory, U.S. Public Health Service, report the results of an investigation of the effect of malaria infection on serological tests for syphilis. At the United States Penitentiary, Atlanta, Georgia, 130 volunteers with no previous history of syphilis and with negative serological reactions were subjected to bites of mosquitoes infected with *Plasmodium vivax*. Blood parasite counts were made daily and blood samples for serological testing were taken about 10 days after maximum parasite counts were obtained. Treponemal immobilizing (TPI) tests were performed concurrently with the serum tests. The serological tests made on all 130 samples of serum were the Kline standard, the Kahn standard, and the V.D.R.L. slide tests, and in addition the Kolmer lipoidal test was performed on 47 samples and the Kolmer cardiolipin antigen test on 49.

False positive findings in titres above the weakly positive or doubtful range were common with the Kahn standard test (94 out of 130) and the Kolmer lipoidal test (22 out of 47). With the Kline, Kolmer cardiolipin, and V.D.R.L. tests the great majority of positive reactions were doubtful or weakly positive. Tests for syphilis using cardiolipin antigens gave fewer false positive reactions than did tests with other antigens. The TPI test in this study showed " poor reducibility," but malarial infection did not seem to have increased the number of false positive reactions. *G. L. M. McElligott*

379. The Incidence and Etiologic Background of Chronic Biologic False-positive Reactions in Serologic Tests for Syphilis: Preliminary Report

J. E. MOORE and C. F. MOHR. *Annals of Internal Medicine* [*Ann. intern. Med.*] **37**, 1156–1161, Dec., 1952. 5 refs.

The authors describe an investigation at the Johns Hopkins University and Hospital, Baltimore, into the incidence and causation of biological false positive reactions to the standard serological tests for syphilis. For this purpose they used the treponemal immobilization (TPI) test to provide confirmation.

Of 300 patients whose serum gave positive reactions to standard serological tests for syphilis, the result of the TPI test was positive in 164 (54·7%) and negative in 136 (45·3%). Of these 136 patients, who were therefore regarded as giving false positive reactions to the serological tests, 51 have so far been subjected to a complete medical survey, including laboratory investigation; some significant abnormality other than the false positive serum reaction was discovered in all but 6. There were 5 cases of collagen disease (disseminated lupus erythematosus, 4; rheumatoid arthritis, 1), and one case each of sarcoidosis, Hodgkin's disease, and Gaucher's disease. In 21 there was historical or clinical evidence which raised strong suspicion that they were suffering from one of the group of collagen diseases (disseminated lupus erythematosus, rheumatoid arthritis, periarteritis nodosa, or rheumatic fever), though in none has the diagnosis yet been fully established, and in 2 others sarcoidosis was suspected. The results of the laboratory tests in most of the 23 patients in this group of " suspects " followed a distinctive pattern. The typical abnormalities consisted of a raised erythrocyte sedimentation rate and a positive reaction to the cephaline cholesterol flocculation test, with sometimes weakly positive thymol-turbidity reactions, elevated serum globulin level, and occasional proteinuria and cylindruria with normal renal function. " L.E." cells were found in the circulating blood only in the cases of characteristic disseminated lupus erythematosus.

It is concluded that the chronic biological false positive phenomenon is far from innocuous, as has hitherto been thought, and is often related to, and may be first evidence of, serious underlying disease. *R. R. Willcox*

380. A Hemolytic Serologic Reaction without Complement as a Possible Test for Syphilis

H. A. COHEN. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **20**, 5–12, Jan., 1953. 4 figs., 4 refs.

The author, working at the Rothschild–Hadassah University Hospital, Jerusalem, has shown that colloidal suspensions of alcoholic solutions of lecithin in saline will haemolyse sheep erythrocytes, and that this lysis is inhibited by sera giving a positive reaction to standard tests for syphilis but not by negative sera. The lytic activity depends both on the concentration of the alcoholic lecithin solution and on the degree of dispersion in saline. Samples of lecithin were found to vary in their activity. The test requires neither complement nor amboceptor.

The antigen is prepared by dissolving egg lecithin in ether, washing with water, and evaporating the ethereal solution to dryness. The residue is dissolved in 96% alcohol to give a 3% solution, 0·9% of cholesterol being added to increase sensitivity. For use, 1 ml. of antigen is mixed with 0·175 ml. of a 1 in 10 dilution of Rein–Bossak cardiolipin antigen in 96% alcohol, 1 ml. of this mixture being then added slowly to 21 ml. of saline. The serum to be tested is inactivated at 56° C. for 30 minutes and the optimum dilution ascertained, that is, the dilution at which a known positive serum completely inhibits lysis, while total lysis occurs with a negative

serum in the presence of enough antigen suspension to lyse double the volume of cells used in the test. [In the protocol showing the optimum dilution the margin of difference between positive and negative sera is very slight; it is not stated whether negative sera show individual variations in titre.]

In setting up the test 0·4 ml. of diluted serum, 0·4 ml. of lecithin suspension, and 1·7 ml. of saline are mixed and incubated for 30 minutes at 37° C.; this is then kept for 19 hours at 4° C. and then for 1 hour at room temperature, after which 0·5 ml. of 2% sheep erythrocyte suspension is added and the degree of lysis read after incubation at 37° C. for 5 minutes.

[No results of serum testing with this technique are given in this preliminary report, as it is emphasized that the test " is not yet sufficiently sensitive or specific ", and therefore " not as yet a practical serologic test for syphilis ".] *A. E. Wilkinson*

381. **The Diagnosis of Early Syphilis during Surveillance of Possible Contacts.** (Le dépistage de la syphilis récente au cours de la surveillance des " contaminations possibles ")
J. PELLEGRIN, –. ISTRIA, and –. MAISONOBE. *Prophylaxie sanitaire et morale* [*Proph. sanit. morale*] **25**, 104–106, April, 1953. 1 ref.

382. **The Treatment of Acute Syphilitic Interstitial Keratitis with Topical Cortisone**
L. C. DREWS, G. D. BARTON, and W. M. MIKKELSEN. *American Journal of Ophthalmology* [*Amer. J. Ophthal.*] **36**, 90–103, Jan., 1953. 8 refs.

The authors, working at the Midwestern Medical Center, St. Louis, Missouri, report the successful results of topical administration of cortisone (drops and/or ointment) in 18 cases of interstitial keratitis. In the majority of cases subjective symptoms were relieved in 3 or 4 days, while signs of active anterior uveitis disappeared in an average of 3 to 4 weeks. There was final visual acuity of 6/9 in 26 out of 29 eyes. Treatment in most cases was continued for an observation period varying between 2 and 16 months. Relapse occurred in 3 cases when cortisone was discontinued after relatively brief periods of treatment, and in one case after 8 months.

[Although it is stated that the recurrence rate with conservative methods is high (15 to 20%), 8 months is an exceptionally long period for one attack. This supports Woods's suggestion that cortisone delays or prevents the development of a natural resistance to the disease.] *A. Lister*

383. **Mass Eradication Treatment of Treponemal Diseases with Penicillin. Laboratory and Clinical Basis for Selection of Effective Schedules**
C. R. REIN and D. K. KITCHEN. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 37–45, Jan., 1953. 6 refs.

In previous work (*J. invest. Derm.*, 1949, **12**, 111) the authors found that the serum concentration of penicillin following single injections of 1·2 and 2·4 mega units of procaine benzyl penicillin in oil with 2% aluminium monostearate (P.A.M.) remained above 0·03 unit per ml. for 6 to 8 days. In the present paper from New York University they specify criteria for a standard preparation, including suspension stability, moisture content, particle size, and diffusion rate in standard cup plate procedure.

The results are reported of the use of this preparation in cases of syphilis, yaws, and pinta, P.A.M. being given either over a period of 2 to 4 days to a total of 1·2 to 2·4 mega units, or in a single injection of 1·2 or 2·4 mega units. The clinical and serological results of these injections were consistently good. It is considered that with this simple, safe, and practical form of ambulatory treatment it should be possible to control the infectious stage and ultimately to eradicate these diseases. *V. E. Lloyd*

384. **Can Anti-syphilitic Treatment of the Mother during Pregnancy Lead to the Development of Non-syphilitic Bone Changes in the Infant?** (Kann eine antiluetische Behandlung der Mutter während der Schwangerschaft zur Ausbildung von nicht-luetischen Knochenveränderungen beim Säugling führen?)
G. GUMPESBERGER. *Dermatologica* [*Dermatologica (Basel)*] **106**, 65–67, 1953. 9 refs.

The question whether specific treatment of the mother for syphilis can affect bone growth in the infant has never been satisfactorily answered. In a study made at the University Skin Clinic, Vienna, 245 infants were examined radiologically during the first month of life for skeletal changes allegedly due to treatment of the mothers, of whom 238 were syphilitic; the 7 non-syphilitic mothers and 43 of the others who had not received any specific treatment during pregnancy, and their infants, acted as a control group.

In all, 80 infants showed non-syphilitic skeletal changes consisting of transverse lines in 74 cases and periosteal thickening in 6. The treatment of the mothers had been with neoarsphenamine and bismuth (100 cases), or with penicillin (62 cases), or with a combination of all three (33 cases). When the different treatment groups were compared with each other and with the untreated group and their 50 infants no clear relationship between the various groups and the skeletal changes could be established. It is thought, therefore, that factors other than specific treatment were responsible for the changes observed, even in those cases showing the so-called " bismuth lines ". *G. W. Csonka*

385. **The Treatment of Syphilis in Pregnancy, using Procaine Penicillin with Aluminium Monostearate Only**
C. K. O'MALLEY. *South African Medical Journal* [*S. Afr. med. J.*] **26**, 1030–1035, Dec. 27, 1952. 7 refs.

Since 1950 the author, at the Peninsula Maternity Hospital, Cape Town, has treated 169 pregnant syphilitic women with procaine penicillin in an oily suspension with aluminium monostearate (P.A.M.). The dosage schedule was 4·8 mega units of P.A.M., given either in 4 injections of 1·2 mega units each at intervals of a week, or in 8 injections of 0·6 mega units twice weekly. The majority of the women were not treated until the last

trimester of pregnancy. A high proportion of the mothers were non-European. Postnatal investigations included a clinical examination and serological tests at the end of the first, second, third, and fourth months after confinement.

The number of infants born to these 169 mothers was 170, but unfortunately a considerable proportion could not be followed up. Of the 170, 8 were stillborn or died soon after birth, and in 2 of these syphilis may have been the cause of death, the mother of one not having completed the schedule of treatment. In 10 infants there was a positive Wassermann reaction at some time or other; 4 of these were not brought back for re-examination and 6 were considered to be non-syphilitic on the basis of subsequent negative reactions.

Altogether the efficacy of the antenatal treatment was assessed in 55 of the 170 infants. In 53 the final status was considered to be satisfactory; in 2 cases treatment failed.

The author considers that the investigation indicates the great value of this method of treatment, but emphasizes the need for a well coordinated plan of treatment and observation, and even suggests that treatment should be compulsory for ignorant and uncooperative people.

(It is of interest to note that 1·5% of European and 8% of non-European pregnant women out of a series of 3,414 gave a positive reaction to the Wassermann test during routine testing.) *Robert Lees*

GRANULOMA INGUINALE

386. **Studies on Granuloma Inguinale. Bacteriologic Behaviour of *Donovania granulomatis***
J. GOLDBERG, R. H. WEAVER, and H. PACKER. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 60–70, Jan., 1953. 6 refs.

Donovania granulomatis was the name given in 1945 by Anderson *et al.* (*J. exp. Med.*, 1945, **81**, 25) to a bacterium isolated from cases of granuloma inguinale. The organism grew only in a medium containing fertile chicken egg-yolk material, and serum from patients with granuloma inguinale contained antibodies against the organism. In this paper the authors, working in the Department of Bacteriology, University of Kentucky, report additional observations on the bacteriology of *D. granulomatis*, and describe their experiments and results in detail.

Four strains of the organism obtained from different laboratories were examined. Morphologically these were found to be very similar, being described as non-motile, pleomorphic, Gram-negative rods about 0·6× 2·0μ in size and usually containing granules, which were frequently bipolar. None of the strains was able to grow on any medium which did not contain egg yolk or some product derived from it. From the outset it was observed that different batches of egg yolk varied in their ability to support growth. Egg yolk from chickens allowed to forage a natural diet for themselves apparently contains a factor which is necessary for the growth of *Donovania*. This factor was absent from the egg yolk of chickens whose diet was regulated in any way. Experiments to determine the nature of this factor showed it to be thermolabile, non-filterable, and capable of being inactivated by diethyl ether, acetone, and ethylene oxide. These latter agents could not, therefore, be used to sterilize a medium designed to grow *D. granulomatis*.

Further experiments showed the growth-promoting factor to be directly associated with the yolk and not a product of embryonic development, since non-fertile chicken, duck, goose, and turkey eggs yielded the factor. In replacement experiments none of the following substances was able to replace the growth factor: haemoglobin, thiamin hydrochloride, tryptophane, cystine, asparagine, biotin, pimelic acid, uracil, adenine, guanine, xanthine, pantothenic acid, rabbit liver extract, yeast extract, and gastric mucin. *Benjamin Schwartz*

387. **Studies on Granuloma Inguinale. The Complement Fixation Test in the Diagnosis of Granuloma Inguinale**
J. GOLDBERG, R. H. WEAVER, H. PACKER, and W. G. SIMPSON. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **37**, 71–76, Jan., 1953. 5 refs.

After a brief review of the literature relating to the complement-fixation test in granuloma inguinale, the authors report the results of their examination at the University of Kentucky of 151 samples of serum from verified cases of the disease in which Donovan bodies had been demonstrated, and of 112 control sera from 55 patients with other venereal diseases, 8 patients with non-venereal diseases, 40 healthy subjects, and 9 patients with lesions resembling granuloma inguinale but in whom *D. granulomatis* could not be demonstrated. All sera were from negroes, since granuloma inguinale affects this race almost exclusively. The antigens used were prepared from bacterial cells of the Anderson and the Georgia strains and culture filtrates from the Anderson strain of organism only; thus each serum was subjected to three tests. Freezing apparently had no effect on the antibody titre of sera.

The results of the various experiments performed are tabulated, and show that of the 151 sera from patients with granuloma inguinale, 136 gave a positive reaction with one or more antigens. The Georgia bacterial antigen was most sensitive, yielding 128 positives, and the Anderson filtrate antigen least sensitive, yielding only 84 positive reactions. All the control sera gave negative results, except one sample from a case clinically resembling granuloma inguinale. A table comparing the results of the tests with the duration of the lesion in positive cases shows that all but one of the sera from patients with granuloma inguinale of a duration of 3 months or more gave a positive test with one or more antigens. The titres of sera increased with the duration of the lesion.

The authors conclude that the results confirm the close association between *Donovania granulomatis* and granuloma inguinale, and suggest that the complement-fixation reaction appears to be a useful diagnostic test.
Benjamin Schwartz

Tropical Medicine

388. **The Inefficacy of Antibiotics in the Treatment of Amoebic Hepatitis.** (Inefficacia degli antibiotici nella terapia dell'epatite amebica)
V. SCAFFIDI and M. SANGIORGI. *Acta medica Italica di malattie infettive e parassitarie* [*Acta med. ital. Mal. infett.*] 7, 281–291, Nov., 1952. 3 figs., 42 refs.

In describing their experience in the treatment of amoebic hepatitis with antibiotics and sulphonamides, the authors include in their series of 11 cases a number in which liquefaction with the formation of an abscess had occurred before treatment, or developed during treatment.

Various drugs were administered, both singly and in combination, and in varying dosage. Of 5 patients with amoebic abscess, one was given sulphathiazole only, another sulphathiazole plus penicillin injected into the abscess cavity, and another parenteral penicillin, with no effect in any of the 3; the fourth was given chloramphenicol, with temporary remission only, and the fifth was given emetine, penicillin, and later aureomycin, but the response was incomplete. There were 4 cases of hepatitis progressing to abscess; in the first of these aureomycin was given without effect on either stage; in the second case chloramphenicol was given at first, with a temporary remission, and in the second stage aureomycin was administered without effect; and in the remaining 2 cases penicillin, streptomycin, chloramphenicol, and aureomycin were all tried without producing more than a temporary remission. Of the 2 patients with non-liquefactive amoebic hepatitis, one was treated with penicillin and one with chloramphenicol, with a temporary remission in each case; but in these cases, as in the others, the final cure was obtained with known amoebicides such as emetine, chloroquine, and "stovarsol" (acetarsol), combined in many cases with aspiration of the abscess. *W. H. Horner Andrews*

389. **Evaluation of Amodiaquin (Camoquin) in the Treatment of Relapsing Vivax Malaria**
J. LOVE, R. FOULK, R. G. W. WILLIAMS, and R. B. MITCHELL. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **225**, 26–33, Jan., 1953. 2 figs., 19 refs.

Camoquin (amiodiaquin), a 4-aminoquinoline compound, was tested therapeutically in 100 consecutive cases of relapsing vivax malaria at the U.S. Naval Hospital, Philadelphia. Most of the patients were members of the armed forces who had recently returned from Korea, where approximately 75% had been taking a suppressive dose of 0·5 g. of chloroquine weekly (though in many cases the drug had been taken irregularly). Twelve patients gave a history of treatment for previous malarial attacks, the average period since the last attack being 5·4 months. Physical examination showed splenomegaly in 34 cases and pharyngitis in 20. Diagnosis was made by examination of both thick and thin blood films.

Camoquin was given as a single oral dose of 10 mg. per kg. body weight (except in one case where the drug was administered rectally, with no difference in response). The temperature rapidly returned to normal (in an average of 18·6 hours) and the patients experienced a rapid and marked subjective improvement. The parasites disappeared from the peripheral blood in the average time of 30 hours, but persisted in 4 cases for 72 hours or more. During a follow-up period of 7 to 9 months the known relapses numbered 20, but more may have occurred; in 3 cases a second relapse occurred, and one case relapsed four times. Relapses occurred after an average of 49·6 days (range 26 to 150 days). Mild nausea and vomiting occurred in 6 cases with the above dosage.

The authors conclude that camoquin is an effective antimalarial drug when given in a single dose, and the relapse rate, although high, is less than that after treatment with chloroquine for 3 days. Mention is made of recent trials of primaquin, an 8-aminoquinoline, which indicate that it is highly effective in preventing relapses when given in a dose of 15 mg. daily for 14 days after curative treatment with camoquin.

W. H. Horner Andrews

390. **Treatment of Acute Malaria with Pyrimethamine**
T. WILSON and J. F. B. EDESON. *British Medical Journal* [*Brit. med. J.*] **1**, 253–255, Jan. 31, 1953. 8 refs.

Pyrimethamine, 2:4-diamino-5-*p*-chlorophenyl-6-ethylpyrimidine, was tried in 126 cases of acute malaria in Malaya. Of 80 patients with falciparum malaria, 15 received a single dose of 50 mg., 39 received two doses, each of 50 mg., and 26 were given 100 mg. on the first day and 50 mg. daily for the next 4 days. The number of cases in each group in which the drug failed to achieve a cure was 2, 4, and 7 respectively; moreover, the drug was slow to control fever and symptoms. Two doses of pyrimethamine, each of 50 mg., were given to 24 patients with proguanil-resistant falciparum malaria. There were 2 immediate failures in this group and one relapse. These results were similar to those obtained in the first group of 80 patients, suggesting that proguanil-resistance does not affect the response to pyrimethamine. The drug was also given to 22 patients with vivax malaria, 11 receiving a single dose of 50 mg. and 11 receiving 100 mg. There were no failures among these patients, but the parasites disappeared slowly from the blood.

The authors consider that pyrimethamine is unsuitable for the treatment of patients with acute malaria due to infection with Malayan strains of *Plasmodium falciparum*.

J. L. Markson

Allergy

391. **The Protective Influence of Graded Doses of Promethazine on Induced Asthmatic Attacks of Graded Intensity**

S. J. Crews and H. Herxheimer. *International Archives of Allergy and Applied Immunology* [*Int. Arch. Allergy*] **3**, 329–333, 1952. 4 figs., 2 refs.

On varying the duration of an inhalation of an antigen aerosol the authors found that an increase in the inhalation time of 20 to 30% did not elicit any response, whereas slightly larger increases sometimes resulted in a severe reaction. There appeared to be a stage at which inhalations produced neither a decrease nor an increase in sensitivity and at which constant responses were obtained with repeated exposures. The authors, at University College Hospital, London, studied the protective effect of promethazine in a pollen-sensitive subject in whom this level was established. They found that a dose which, given before the test, protected the subject against an inhalation lasting 60 seconds failed to protect against one lasting 70 seconds, at which point a larger dose of promethazine was effective, and this in turn became ineffective on increasing the duration of exposure. Thus there was a step-like relation between the dose of the antihistamine capable of protecting the subject and the size of dose of the inhaled allergen.

J. Pepys

392. **Pulmonary Function Studies in Bronchial Asthma. I. In the Control State**

J. A. Herschfus, E. Bresnick, and M. S. Segal. *American Journal of Medicine* [*Amer. J. Med.*] **14**, 23–33. Jan., 1953. 8 figs.

There have been many studies of pulmonary function in patients with emphysema, fibrosis, or tuberculosis, but few in patients with classic bronchial asthma. At Tufts Medical College and the City Hospital, Boston, the authors carried out pulmonary function tests on 42 patients suffering from the perennial type of asthma, at times when the subjects felt fit and were fairly free from wheezing. The technique used is described in detail.

The vital capacity was found to vary appreciably in the same patient even in the absence of wheezing, the range being from 51% to 158% of the predicted normal value, with an average of 100·1%. It was lower during attacks of asthma. Inspiratory capacity volume and expiratory reserve volume were reduced, the former from the normal of between 75 and 80% to 68%. The maximum breathing capacity of control subjects was 106·3% against 62·9% in 39 asthmatics, only 5 of the latter giving normal results. The index of intrapulmonary mixing in normal individuals was up to 2·5% of nitrogen after breathing oxygen for 7 minutes, but in the asthmatics the range was from 1% to 12·12% and the average 4·05%, increasing to 5·34% with mild wheezing. The total lung capacity, calculated on the maximum recorded vital capacity, was 125·8% of the predicted value, against 120·8% in controls. Although the residual volume varies considerably in different persons, its relation to the total lung capacity is normally fairly constant at 20% to 30·8%; in asthmatics it was consistently raised to 45% to 48%.

Arterial oxygen saturation was measured in 15 cases but, as was to be expected in the absence of bad asthma or emphysema, was low in only 3 cases. The maximum expiratory velocity was measured with a bobbin flowmeter; in normal subjects it was 8 to 10 litres per second, while the average in asthmatics was only 3·9 litres per second. [Alternatively the expiratory rate may be calculated from the spirometer tracing of the vital capacity, the time factor being ignored if the total volume alone is noted.] These studies show that the total lung capacity rises, and the maximum breathing capacity falls and its duration increases, with the severity of the asthma; even in the asymptomatic state the maximum breathing capacity averaged only 75% of normal. The tests also demonstrated impaired lung function in the absence of severe wheezing. *K. Gurling*

393. **Pulmonary Function Studies in Bronchial Asthma. II. After Treatment**

J. A. Herschfus, E. Bresnick, and M. S. Segal. *American Journal of Medicine* [*Amer. J. Med.*] **14**, 34–40, Jan., 1953. 2 figs., 42 refs.

The lung function tests described in the previous paper [Abstract 392] were repeated after the administration of 0·5 g. aminophylline intravenously, and 6 inhalations of a 2·5% isoprenaline spray.

The vital capacity increased by 10·6% after aminophylline and by 16·9% after isoprenaline, and the maximum breathing capacity by 30·9% and 50% respectively even in the absence of wheezing, but normal values were never reached. Resting ventilation increased very slightly, but the index of intrapulmonary mixing fell from 4·05% of nitrogen to 2·22% after aminophylline and 2·97% after isoprenaline. The average total lung capacity increased insignificantly, and the relation of residual volume to total lung capacity fell by 7 or 8% with both forms of treatment. The maximum breathing velocity increased by 30·6% after aminophylline and 58·5% after the spray. The significance of these changes is discussed in relation to symptomatic improvement, and it is suggested that reduction in bronchial spasm is of more importance than either reduction in pulmonary blood flow or increase in " collateral respiration " by the release of blocked bronchioles. *K. Gurling*

394. **Allergic Manifestations in the Gastrointestinal Tract**

A. F. R. Andresen. *Gastroenterology* [*Gastroenterology*] **23**, 20–35, Jan., 1953. 23 refs.

Nutrition and Metabolism

395. **Food Supply, Body Weight, and Activity in Great Britain, 1943–9**

J. M. HARRIES and D. F. HOLLINGSWORTH. *British Medical Journal* [*Brit. med. J.*] **1**, 75–78, Jan. 10, 1953. 3 figs., 18 refs.

Average figures for the body weight of adults and for food intake (from the National Food Survey) have been recorded by the British Ministry of Food for 10 years or more. In this paper, the authors study the relation of the weight of male and female industrial workers and of housewives to the caloric intake of urban working-class households for the period 1943–9.

It was found that these two sets of data showed parallel changes. There were three phases in the average daily caloric intake: (1) an increase of 140 Calories from April, 1943, to early 1945; (2) a fall of 120 Calories from early 1945 to early 1947; and (3) a rise of 120 Calories from early 1947 to the end of 1949. For the corresponding periods the changes in weight were: (1) an increase of 1½ lb. (680 g.) for men and 3 lb. (1,360 g.) for women; (2) a decrease of 1 lb. (454 g.) for men and ½ lb. (227 g.) for women; and (3) an increase of 2 lb. (907 g.) for men and 3 lb. (1,360 g.) for women. The loss in weight was greatest among housewives and workers without access to canteens, and least among workers with access to canteens, in some of whom there was even a slight gain in weight. Records of weights of children, published, for example, by school medical officers, showed a comparable regression in growth rate in 1946 and 1947.

The authors give reasons for supposing that bodily activity in the adults did not alter much in the years surveyed so that they regard the changes in weight as due to changes in caloric intake. They conclude that 2,900 Calories probably reflects the average caloric need of these groups better than the earlier figure of 2,800 arrived at in 1944. They also suggest that, since no measurable ill effects to health accompanied the observed fall in weight, the measurement of body weight may offer an earlier indication of the inadequacy of food supplies than clinical examination. *John Yudkin*

396. **Dextran as a Source of Liver Glycogen and Blood Reducing Substance**

W. E. BLOOM and A. E. WILHELMI. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **81**, 501–503, Nov., 1952. 3 refs.

Previous studies having shown that dextran given to human subjects is not recovered in the stools, and various theories having been propounded to explain its disappearance, these further experiments were carried out by the authors at Emory University School of Medicine, Georgia. Fasting male rats were given 5 ml. of 18% dextran in 0·9% saline solution by stomach tube. The amount of reducing substance in the blood was significantly increased one hour after ingestion of the dextran and was still raised after 4 hours; this reducing substance was shown to be entirely fermentable or nearly so. Liver glycogen, determined by means of the anthrone reaction, was also considerably increased 4 hours after giving dextran. When liver samples were allowed to stand for 2 hours at room temperature most of this glycogen disappeared. The increase in apparent glycogen is therefore not due to dextran deposition in the liver, since added dextran did not undergo such disappearance at room temperature. Similar results were obtained in 4 human subjects given 100 ml. or 200 ml. of 20% dextran by mouth, blood sugar levels being determined ½, 1, and 2 hours thereafter.

The authors conclude that dextran is rapidly broken down in the intestine to products yielding glucose and glycogen, and that this process is most probably due to the action of an enzyme or enzymes. Further experiments to confirm this are in progress. *C. L. Cope*

397. **Further Studies of the Effects of Citrate Feeding on the Calcium, Phosphorus, and Citrate Metabolism of Rachitic Infants**

H. E. HARRISON and H. C. HARRISON. *Journal of Pediatrics* [*J. Pediat.*] **41**, 756–765, Dec., 1952. 3 figs., 15 refs.

These observations were made at Johns Hopkins University and Baltimore City Hospital on 3 infants suffering from rickets, in an effort to explain the antirachitic effect of citrates. The infants were kept on a constant diet low in vitamin D, consisting of cow's milk, cereals, vegetables, and ascorbic acid; an equimolar mixture of citric acid and trisodium citrate in amounts from 30 to 60 mM. of citrate per day was added to the milk feeds. Calcification of rachitic bone matrix could be demonstrated radiologically in all 3 cases when adequate amounts of citrate were given, in spite of persistently low concentrations of calcium and phosphorus in the serum and also in the intracellular fluid. These levels were considered to be too low for the deposition of bone salts. Although the quantity of citrate administered would alter the solubility of calcium and phosphorus, thus promoting their increased absorption, the findings in this series did not show any evidence of such an effect. The rapid decrease of serum calcium levels after the beginning of citrate therapy, together with the persistently low serum phosphorus concentration and the maintenance of serum citrate concentration at a level corresponding to that before citrate therapy, suggest that calcium salts are deposited at a higher rate than that of intestinal absorption of calcium.

The authors suggest, therefore, that the antirachitic effect of citrate is not due to the formation of a more diffusible calcium–citrate complex, but rather to some local action upon the bone matrix resulting in " increased calcifiability ". They point out that a similar sequence of events may be observed after removal of hyper-

functioning parathyroid tissue, when the decalcification of the skeleton is followed by mineralization, as occurred in the citrate-fed rachitic infants; in both instances this is associated with decreased serum calcium and phosphorus levels. It is, so far, not known whether prolonged citrate therapy would be a complete substitute for the administration of vitamin D in the prevention and treatment of rickets. *Z. A. Leitner*

398. **Removal of Calcium in Man by Ethylenediamine Tetra-acetic Acid. A Metabolic Study**
H. SPENCER, V. VANKINSCOTT, I. LEWIN, and D. LASZLO. *Journal of Clinical Investigation* [*J. clin. Invest.*] **31**, 1023–1027, Dec., 1952. 2 figs., 10 refs.

The effect of the salts of ethylenediamine tetra-acetic acid on calcium metabolism was studied at Montefiore Hospital, New York, on 11 patients, the sodium salt being used on 10 occasions and the calcium salt on 5. Two of the patients were suffering from osteoporosis, 2 had osteoblastic metastases from carcinoma of the prostate, 2 had osteolytic metastases from carcinoma of the breast, one had multiple myeloma, and 4 had no bone disease. In the majority of cases 4 g. of the salt made up into a 20% solution was added to 500 ml. of 5% glucose solution and infused over a period of 6 hours. There was no significant change in the calcium content of the faeces, but excretion in the urine was increased by 45 to 72% over the expected value in the case of the sodium salt and by 63 to 88% in the case of the calcium salt, the excess being considerably greater than that observed after the administration of an equivalent amount of calcium gluconate. The only clinical abnormality resulting from the injection was a lowering of the systolic blood pressure in two-thirds of the cases. The serum calcium level as determined by the oxalate precipitation method was not significantly altered during or after the infusion of the sodium salt, but the total calcium content of the acid ashed serum was increased, the difference (the maximum value of which was 4·3 mg. per 100 ml.) being due to binding of calcium by the ethylenediamine tetra-acetic acid.

The authors conclude that ethylenediamine tetra-acetic acid causes demineralization of the skeleton, the effect being dependent on the rate of infusion and the total quantity of the reagent administered rather than on the state of the skeletal system. The lack of reduction in serum calcium level indicates prompt replenishment by mobilization of ionized calcium from the skeletal deposits. The marked effect of the calcium salt suggests its employment to remove minerals, such as radium and lead, deposited in the bones. *R. E. Tunbridge*

399. **Postoperative Water and Sodium Retention**
L. P. LE QUESNE and A. A. G. LEWIS. *Lancet* [*Lancet*] **1**, 153–158, Jan. 24, 1953. 6 figs., 33 refs.

Water and electrolyte balance before and after operation was studied at the Middlesex Hospital, London, in a group of 21 surgical patients, 19 of them undergoing partial gastrectomy for benign peptic ulceration, one excision of the sigmoid colon for carcinoma, and one inguinal herniorrhaphy. The investigations were made for 3 to 4 days before the operation and for 1 to 8 days afterwards. An "almost constant" food and water intake was assured preoperatively by giving a standard mixture of "casinal" (calcium caseinate), glucose, arachis oil, and ascorbic acid in 3 litres of water by slow drip down a Ryle's tube and allowing only 1 litre of water by mouth; and postoperatively by giving intravenous fluids until the preoperative regimen could be resumed. In respect of daily electrolyte intake the patients were divided into three groups: (1) receiving 160 to 170 mEq. of sodium chloride throughout; (2) receiving no sodium from the day of the operation onwards; and (3) receiving the same amount of sodium chloride as Group 1 and also 100 mEq. of potassium (except on the day of the operation, when this amount was halved).

On studying the results three clearly separable phases were observed in the postoperative period: (*a*) primary water retention, which rarely lasted more than 24 hours; (*b*) early sodium retention, also in the first 24 hours; and (*c*) late sodium retention, starting 24 to 48 hours after operation and lasting several days. The retention of salt and water may be continuous or interrupted, depending on the relationship of the last two. The primary water retention was found to be independent of sodium retention, and appears to result from the release of pituitary antidiuretic hormone caused by such stimuli as emotion, trauma, and drugs. Early sodium retention may be caused, at least in part, by hypotonicity of the blood resulting from water retention during the early part of the day of operation. Adrenocortical release is probably responsible for the late sodium retention and also, in part, for the early retention of this electrolyte.
A. Swan

400. **Uric Acid Production in Normal and Gouty Subjects, Determined by N^{15} Labeled Glycine**
A. F. MULLER and W. BAUER. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **82**, 47–50, Jan., 1953. 2 figs., 7 refs.

By administering glycine labelled with radioactive nitrogen (^{15}N) and subsequently measuring the concentration of the isotope in the urinary uric acid in 2 normal subjects and one patient with gout, Benedict *et al.* (*Metabolism*, 1952, **1**, 3) showed in the gouty subject that the high blood content of uric acid was due to increased uric acid production. This patient was exceptional, however, in having a high urinary output of uric acid and only minor tophaceous involvement. At the Massachusetts General Hospital the present authors, using a similar technique, have therefore studied a gouty subject with high blood uric acid content, normal renal function, and normal uric acid excretion, and a healthy control subject, both of whom were taking a low-purine diet. The cumulative excretion of ^{15}N in urinary uric acid was similar in the two subjects, as also was its concentration in specimens taken on each of the 10 days after its administration, except for a sharp rise and fall on the 2nd and 3rd days in the case of the gouty patient. The authors therefore suggest that an increased production of uric acid does not appear to be an essential feature of gout. *K. G. Lowe*

Gastroenterology

STOMACH AND DUODENUM

401. The Electrógastrograph: Some Clinical Applications

H. S. MORTON and W. S. MARTIN. *Review of Gastroenterology* [*Rev. Gastroent.*] **20**, 37–53, Jan., 1953. 14 figs., 37 refs.

By means of a small silver–silver-chloride electrode in the stomach and an electrode on the skin, electrical potentials generated by gastric function may be detected, which are amplified and recorded by an instrument called the "electrogastrograph". Two types of electrical change are found: (1) a steady potential difference due probably to the secretory activity of the cells of the gastric mucosa and varying, in a series of normal subjects, between −10 mV and −25 mV (average −15 mV); (2) smaller alternating waves due to muscular activity, which consist of a basic pattern of slow waves (3 per minute) on which are superimposed smaller waves of higher frequency.

In 20 cases of duodenal ulcer the steady potential difference was found to average +10 mV, and the small alternating waves were increased in amplitude and frequency. One supposedly healthy control subject was found to have a high potential, and 6 months later developed a duodenal ulcer which was diagnosed radiologically. Acute gastric erosions gave a similar electrogastrographic picture to that of duodenal ulcer. In cases of carcinoma of the stomach recordings of low activity have been found, with irregular spikes of potential, but as yet no specific pattern has been identified. Certain drugs have a constant effect, histamine (0·25 mg.) causing a rise of 5 mV and atropine and "banthine" (methantheline) causing a depression of potential and a slowing of the wave pattern. Banthine given therapeutically for duodenal ulcer reduces the potential to within normal limits.

A. G. Parks

402. Treatment and Prognosis of Acute Perforated Peptic Ulcer

F. AVERY JONES and R. DOLL. *British Medical Journal* [*Brit. med. J.*] **1**, 122–127, Jan. 17, 1953. 9 refs.

During the last 10 years there has been a remarkable fall in operative mortality in cases of perforated peptic ulcer, which the authors attribute mainly to the advent of antibiotics and to the use of muscle relaxants in surgery. This improvement was demonstrated in a series of 490 cases treated at the Central Middlesex Hospital, London, in 1938–48, an analysis of which has been published previously (Avery Jones *et al.*, *Brit med. J.*, 1950, **1**, 211; *Abstracts of World Surgery*, 1950, **8**, 72). In the present paper this analysis has been extended to include a further 3 years, the whole series now totalling 715 patients treated during the period 1938–51, with the objects of determining: (1) whether the fall in fatality rate has continued; (2) how the results of surgical closure of the perforation compare with those obtained by other methods; (3) whether indications for the employment of the different methods of treatment can be defined.

Since the beginning of 1947 no recognizable change in fatality rate could be found. The over-all fatality rate in 320 patients treated during the 5 years 1947–51 was 7·9%, and the operative mortality in 320 cases was 31%. As far as the second question is concerned, the authors' data do not permit any comparison of the results of surgical and medical treatment, as the latter was mainly confined to patients who were too ill for surgery. Nor can the relative merits of simple closure and immediate partial gastrectomy be assessed, as although 19 patients were treated by partial gastrectomy without fatality, bad-risk cases had been excluded from this group. Regarding the third question, the authors consider that simple closure of the perforation is the treatment of choice in the majority of cases of perforated duodenal ulcer. Immediate partial gastrectomy is to be preferred in all cases of perforated gastric ulcer, provided the surgeon is experienced in the technique, owing to the considerable risk of malignant change even in an ulcer that appears simple at operation. It is also the treatment of choice for any case in which perforation is associated with haemorrhage as there is a definite tendency for bleeding to recur, and for cases in which there is a history of dyspepsia of more than 1 year's duration—especially if a definite diagnosis of ulcer has been made on a previous occasion—as the authors' figures show that a high percentage of such patients will require further operative treatment later if the immediate treatment has been confined to simple closure of the perforation. As for medical treatment, the authors associate themselves with Tanner's view that it is unsuitable for routine use, being safe only in the hands of the enthusiast.

R. Schneider

403. Endoscopic Aspects of the Gastric Mucosa in Relation to its Function. Part I. In the Gastritides

S. J. STEMPIEN, J. E. ORITT, and N. W. KARR. *Gastroenterology* [*Gastroenterology*] **23**, 45–54, Jan., 1953. 5 figs., 10 refs.

The pathology of the gastric mucosa in relation to hydrochloric acid secretion is discussed in this paper from the Veterans Administration Hospital, Long Beach, California. Biopsy material from the gastric mucosa in 450 cases was examined histologically and divided into 5 diagnostic groups: (1) normal gastric mucosa, (2) superficial gastritis, (3) atrophic gastritis, (4) hypertrophic gastritis, and (5) mixed gastritis. Gastric analyses were carried out after the injection of 0·5 mg. of histamine subcutaneously, and the highest acid value in Töpfer units was recorded. Cases in which there were other lesions, such as gastric ulcer or carcinoma, were excluded.

The free hydrochloric acid response of normal gastric mucosa varied widely; achlorhydria was noted in 11 cases out of 146 in this group. The authors infer that normal gastric mucosa undergoes states of hypersecretion and hyposecretion without visible evidence of pathological change. In most of the cases of severe superficial gastritis and of severe atrophic gastritis there was anacidity. In the hypertrophic group the most striking finding was the total absence of anacidity; in this group also there was a larger number of cases with a high acid secretion. The findings in the mixed gastritis group were not statistically significant.

The authors conclude that hypertrophic gastritis is correlated with hyperfunction of acid secretion and atrophic gastritis with hypofunction. [See Abstract 404.] *I. McLean-Baird*

404. **Endoscopic Aspects of the Gastric Mucosa in Relation to its Function. Part II. In Benign Gastro-duodenal Ulcer**

S. J. STEMPIEN, J. E. ORITT, and N. W. KARR. *Gastro-enterology* [*Gastroenterology*] **23**, 55–59, Jan., 1953. 3 figs., 7 refs.

In the second part of this paper the authors attempt to show whether the relationship of atrophic gastritis with hypoacidity and of hypertrophic gastritis with hyper-acidity [see Abstract 403] still holds true in the presence of gastric or duodenal ulcer. A subcutaneous injection of 0·5 mg. of histamine was given to 62 patients with proved gastric ulcer and 53 with duodenal ulcer. Gastric analysis with Töpfer's reagent was carried out ½ and 1 hour after the injection of histamine.

Atrophic gastritis was observed in 18 of the patients with gastric ulcer but in only 6 of those with duodenal ulcer; evidence of hypertrophic gastritis was found in 20 of the patients with duodenal ulcer and in 11 of those with gastric ulcer. Normal mucosa and mixed gastritis were observed about equally in both groups. Gastric ulcer was more frequently associated with hypoacidity and duodenal ulcer with hyperacidity. There was no case of anacidity in the duodenal ulcer group, whereas in the gastric ulcer group there were 11 cases of histamine-fast achlorhydria.

The authors conclude that in cases of benign gastric ulcer or anacidity hypoacidity commonly occurs and is the result of superficial and atrophic gastritis; in cases of duodenal ulcer there is hypersecretion, which is a reflection of an associated hypertrophic gastritis.

I. McLean-Baird

405. **Heidenhain Pouch Secretory Response as Affected by Gastrojejunostomy to the Main Stomach**

E. J. SCHMITZ, E. A. KANAR, E. H. STORER, L. R. SAUVAGE, and H. N. HARKINS. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **81**, 170–172, Oct., 1952. 1 fig., 2 refs.

Working at the University of Washington School of Medicine, Seattle, the authors have studied experimentally the acid secretory response of the gastric mucosa to gastro-jejunostomy. In dogs Heidenhain-type (vagally denervated) pouches of the stomach were constructed and the 24-hour secretion was estimated for 30 days after a 2-week recovery period. The daily average output of free hydrochloric acid (HCl) was 35 mEq. A short-loop, antecolic, isoperistaltic gastro-jejunostomy, situated 6 to 7 cm. proximal to the pylorus at the most dependent part of the stomach was then carried out, and gastric secretion again estimated for 30 days after 2 weeks' rest. The daily average output of free HCl was now 85 mEq., with greater daily variations than before operation. The anastomosis was removed in 2 dogs and the secretion estimated postoperatively, as before. Output of free HCl in the 2 animals averaged about 64 and 25 mEq. respectively per day, although daily variations were greater than before the gastro-jejunostomy was performed.

It is suggested that one cause of the higher output of HCl after gastro-jejunostomy is increased neutralization of gastric contents or repeated stimulation of the pyloric antrum by circulation of gastric contents between pylorus and stoma. [The authors do not mention, however, the possibility that the extent of the " intestinal phase " of gastric secretory stimulation by food may be increased by the operation.] *R. A. Gregory*

LIVER AND GALL-BLADDER

406. **The Radiological Anatomy of the Intrahepatic Bile Ducts.** (Anatomie radiologique des voies biliaires intrahépatiques)

M. ROUX, E. BERNIER, C. DEBRAY, R. LE CANUET, and J. GARRET. *Journal de Chirurgie* [*J. Chir. (Paris)*] **69**, 5–18, Jan., 1953. 14 figs., 6 refs.

At the Laboratory of Experimental Surgery, Paris, the authors have conducted radiological investigations on the intrahepatic biliary tracts in 34 cadavers, both with the liver *in situ* and exteriorized. They have shown that the drainage from the right and left lobes of the liver is completely separate; that from the right lobe is through two chief tributaries, one antero-superior and the other postero-inferior, the antero-superior duct being the bigger, having a more extensive arborization, and being in the direct line of the right hepatic duct; the postero-inferior branch usually joins the left border of the antero-superior after describing a curve which is concave below. Occasionally, this branch is double, and more rarely it may join the left hepatic duct, an anomaly which is important to the surgeon and may be suspected if the origin of the common bile duct lies at a little distance from the porta hepatis. There is a third tributary to the right hepatic duct, which the authors term the intermediate branch. This usually drains into the antero-superior branch.

In the left lobe of the organ the arrangement is much more simple and consists of two tributaries with peripheral dichotomy.

The plane of cleavage or boundary fissure between the right and left lobes of the liver was found to run obliquely from above downwards and from left to right antero-posteriorly, at an angle of 35 degrees to the sagittal axis.

Radiographs of the lateral view demonstrated that the right lobe was situated posteriorly. These arrangements explain why an operative cholangiogram fills chiefly the postero-inferior tributaries of the right hepatic duct and seldom shows up the left hepatic duct.

K. Whittle Martin

407. **Cholecystectomy and its Relation to the Stomach and Duodenum. Review of 75 Cases with Preoperative and Postoperative *X*-ray Studies**

R. E. ROTHENBERG. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **96**, 421–426, April, 1953. 14 figs.

408. **The Indications for Various Types of Surgical Intervention in Choledocholithiasis.** (Les indications respectives des diverses interventions dans la lithiase cholédocienne)

P. MALLET-GUY and M. GANGOLPHE. *Mémoires de l'Académie de chirurgie* [*Mém. Acad. Chir.* (*Paris*)] **79**, 60–68, Jan. 14, 1953.

In dealing with stone in the common bile duct the authors strongly advocate the preliminary determination of the amount of biliary obstruction by radiographic and manometric methods at the time of operation. In this article conclusions are drawn from the study of 100 patients treated in this manner by one of the authors during the course of 2 years, among whom there were more than the average number of severe cases, while 28 were over the age of 65 years. In 30 cases stones were found in the common bile duct in the absence of any clinical indications pointing in that direction; in 13 of these no stone could be felt on careful palpation of the duct, and its presence would not have been suspected had not radiographic and manometric investigation been carried out as a routine procedure.

The authors estimate the likely risk of operation by taking into consideration four factors: (1) the general constitution (age, presence of any associated disease); (2) the general effects of the biliary disease (loss of weight, anaemia, deficiency of blood protein); (3) hepatic function; and (4) the condition of the biliary passages. By means of these criteria they divide the 100 patients into three groups according as the operative risk was estimated as moderate (42), considerable (31), or serious (27).

In treatment, every effort was made to maintain two principles: (*a*) to do all that was necessary in one operation, and (*b*) to avoid, so far as was possible, external drainage of the common bile duct. In 19 cases all drainage was dispensed with; in 4 of these the common duct was incised and sewn up, while in 15 the stone was extracted through the end of the cystic duct, which was then ligated; there was one death in this group. In 11 cases the stone was removed through a duodenal incision, there being one death in this group. In 54 cases the common bile duct was anastomosed to the duodenum; although these were more serious cases, there were only 5 deaths. External biliary drainage was employed in only 16 cases; there were 2 deaths, both from among those patients in whom the risk was considered more serious.

(In the discussion which followed the reading of the paper several surgeons supported the views expressed by the authors, but one speaker stated that he considered simple drainage of the biliary tract was sometimes life-saving as a preliminary to a more radical operation.)

Zachary Cope

INTESTINES

409. **The Treatment of Steatorrhoea in Crohn's Disease**

J. BURKE. *British Medical Journal* [*Brit. med. J.*] **1**, 239–242, Jan. 31, 1953. 13 refs.

The author reports from the Royal Infirmary, Sheffield, 3 cases of regional ileitis, in all of which steatorrhoea, malnutrition, and hypochromic anaemia were prominent features. Considerable improvement followed the administration of a high-protein diet (about 130 g. of protein daily). Administration of iron intravenously was also beneficial to these 3 patients. As the presence of steatorrhoea in Crohn's disease is often overlooked, regular estimation of the faecal fat content in this condition is recommended.

A. C. Frazer

410. **Ion-exchange Resins as Adjuncts in Treatment of High Intestinal Fistulae. Clinical and Experimental Study**

B. EISEMAN and H. E. STEPHENSON. *Archives of Surgery* [*Arch. Surg.* (*Chicago*)] **65**, 871–875, Dec., 1952. 6 refs.

411. **Terminal Lymphoid Ileitis.** (L'iléite lymphoïde terminale)

G. ARNULF and P. BUFFARD. *Presse médicale* [*Presse méd.*] **61**, 107–109, Jan. 28, 1953. 7 figs.

In this interesting paper from the Clinique Claude-Bernard, Lyons, the authors report a series of nearly 100 cases of non-specific mesenteric adenitis. In the course of 1,307 explorations of the right iliac fossa they found 98 cases of primary mesenteric adenopathy with a healthy appendix, only one of which turned out to be tuberculous. They assert that the primary lesion in this type of case is in the lymph follicles of the terminal ileum, and they have been able to demonstrate important characteristic *x*-ray appearances, the swollen follicles causing small, oval filling defects and sometimes visible ulceration.

The patients in this series were nearly all between 5 and 15 years of age, there being only 3 adults. The condition may be acute or chronic, the former being characterized by pyrexia of 39° to 40° C. (102 to 104° F.) with pain in the right iliac fossa, sometimes colicky, but without rigidity; in the chronic form the pain is intermittent and may recur over a period of months. In both types there is tenderness, sometimes with an ill-defined mass, in the iliac fossa, but both pain and tenderness are more medial than is usual in appendicitis, being juxta-umbilical. In spite of exhaustive investigations, no specific causitive organism could be isolated in any of the authors' cases, and they believe faecal organisms to be responsible, as in appendicitis.

The condition responds to chemotherapy with antibiotics and, in particular, with sulphonamides in a

spectacular fashion, but operation is advised since only thus can appendicitis be excluded. At operation the mesentery is found to be oedematous and slightly reddened, there is often a little fluid and sometimes fine pericaecal adhesions, and the mesenteric lymph nodes are enlarged, but the appendix is normal. After the diagnosis has been established, sulphonamides are given.

H. Daintree Johnson

412. **Results in the Treatment of Carcinoma of the Colon and Rectum. An Analysis of 2,341 Cases over a 35 Year Period with 5 Year Survival Results in 1,667 Patients**
R. S. GRINNELL. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **96**, 31–42, Jan., 1953. 4 figs., 22 refs.

The results of treatment of 890 patients with carcinoma of the colon and 777 patients with carcinoma of the rectum admitted to the Presbyterian Hospital, New York, from 1916 to 1945 inclusive have been presented. These were patients who had not had previous curative treatment.

The resectability rate for colon tumors rose from 50% for the 1916 to 1920 period to 92·1% for the 1945 to 1950 period and the operative mortality fell from 31·3 to 5·3% for these same periods. For rectal tumors the resectability rate rose from 65·7% to 83·3% and the operative mortality fell from 40·9 to 6·7%.

The absolute 5 year survival rate for patients with carcinoma of the colon admitted to hospital from 1916 to 1945 inclusive was 25·6%. During the 1941 to 1945 period there was a decrease in the survival rates of both the colon and rectal groups.

The relative 5-year survival rate for patients undergoing curative colon and abdominoperineal resection from 1916 to 1945 was 45·5 and 46·4% respectively. In both colon and rectal groups during the 1941 to 1945 period there was a decrease in the survival rates of those patients who survived the operation. The 5 year results following curative colon resection were very similar for the right and left colon. The poorest results were in tumors of the hepatic flexure because of an early spread to the liver and the duodenal area. The resectability rate of these tumors was also much lower than for other segments of the colon.

The 5 year survival rate for patients who were treated by curative colon resection from 1936 to 1945 and survived operation was 67·9% for those without node metastasis in the resected specimens and 36·7% for those with node metastasis. The rate for patients treated by curative abdominoperineal and perineal proctectomy was 67·4% for those without metastasis and 34·6% for those with metastasis.

There was no evidence found in a study of the 5 year results that the chances of survival following curative colon resection or curative abdominoperineal resection were less in the younger age group.

The 5 year survival rate for 53 patients with carcinoma of the rectum treated by colostomy and perineal proctectomy from 1916 to 1945 was 32·1%. The rate was approximately 13% lower than that following abdominoperineal resection over a similar period.

Although the absolute 5 year survival rate of patients with large bowel cancers has risen in the past 30 years, chiefly because of the rise in resectability and the fall in operative mortality, there is little evidence in the bare percentages themselves of any recent improvement in our surgical attack on the cancer itself. The actual drop in the survival rate in the last 5 year period, especially in rectal cancers, suggests that our treatment has been less effective than previously. The actual decline in the survival rate of operative survivors in 1941 to 1945 following curative colon and abdominoperineal resection may be caused in part by attempting curative resections on advanced tumors which in reality were not curable by surgery. We should not be deterred, however, from continuing to do radical resections on tumors whose curability is undetermined.—[Author's summary.]

413. **The Ano-sigmoid Inhibitory Reflex.** (Le réflexe ano-sigmoïdien inhibiteur)
C. DEBRAY, F. PERGOLA, and J. AUBRION. *Archives des maladies de l'appareil digestif et des maladies de la nutrition* [*Arch. Mal. Appar. dig.*] **42**, 5–11, Jan., 1953. 3 figs.

A simple method of recording variations of pressure within the sigmoid colon is described. The tracing obtained in normal adults shows waves of contraction occurring at a rate of approximately 2 to 3 per minute and having a pressure of 10 to 15 cm. of water. When the anal canal was stimulated by the introduction of a glass rod, or by the inflation of a balloon inserted just above the sphincter, the contractions of the sigmoid colon ceased immediately and a fall in the muscular tone occurred within 30 to 60 seconds; after a lapse of approximately 1 to 3 minutes the contractions reappeared and the tone was restored; each subsequent stimulation of the anal canal was followed by an inhibition of contractions and tone in the sigmoid colon.

The authors conclude that these findings derive from a reflex mechanism, the ano-sigmoid inhibitory reflex, which is initiated in the mucous membrane of the anal canal, or in the sphincter muscle, or in both. This reflex is considered to be important in the physiological maintenance of rectal continence; pathologically, its persistence may afford a partial explanation of the mechanism of certain types of constipation.

Joseph Parness

414. **Statistical Notes on 4,485 Patients Operated upon for Acute Appendicitis.** [In English]
H. L. M. VAN DER HOFF. *Archivum Chirurgicum Neerlandicum* [*Arch. chir. neerl.*] **4**, 291–303, 1952.

An analysis is presented of a series of 4,485 cases of acute appendicitis treated during the period 1925–50. The frequency of mistakes in diagnosis was about 10%, the exact figure depending on the criteria employed in labelling the removed appendix as pathological. In the pre-antibotic era the over-all mortality was 1·4% (but 7·6% in 593 cases in which perforation had occurred). It was significantly higher in men than in women, and postponement of operative measures after perforation coincided with an increase in mortality.

Guy Blackburn

Cardiovascular System

415. **Arrhythmias Produced by Intravenous Procaine Amide**
L. J. ACIERNO, R. GUBNER, and B. POLIAKOFF. *New York State Journal of Medicine* [*N.Y. St. J. Med.*] **53**, 72–74, Jan. 1, 1953. 2 figs., 3 refs.

The authors describe 2 cases, seen at Kings County Hospital, Brooklyn, N.Y., in which ventricular arrhythmia followed intravenous administration of procainamide. In the first case, that of a young man who developed ventricular tachycardia as a result of phosphorus poisoning, bundle-branch block and cardiac arrest were observed after injection of 300 mg. of procainamide over a period of 8 to 10 minutes. Although the patient was moribund when the drug was given, the changes in the electrocardiogram indicated that procainamide accelerated death. In the second case, that of a man of 72 with bundle-branch block and tachycardia of uncertain type after myocardial infarction, short paroxysms of ventricular tachycardia and auricular flutter developed during administration of 600 mg. of procainamide over a period of 35 minutes. The electrocardiogram revealed slowing of the flutter waves as a result of the procainamide. The ventricular tachycardia disappeared when digitalis was given, but the auricular flutter persisted. The patient recovered, the ventricular rate being controlled by digitalis throughout his stay in hospital.

The authors point out that the disturbances in rhythm and conduction after administration of procainamide are similar to those which may occur after the intravenous injection of quinidine. Great caution should be exercised in the administration of procainamide intravenously, only small divided doses being given at one time. Cardiographic and blood pressure recordings should be taken continuously. *J. F. Goodwin*

416. **Right Auricular and Ventricular Pressure Patterns in Constrictive Pericarditis**
P. N. G. YU, F. W. LOVEJOY, H. A. JOOS, R. E. NYE, and E. B. MAHONEY. *Circulation* [*Circulation (N.Y.)*] **7**, 102–107, Jan., 1953. 5 figs., 4 refs.

At the University School of Medicine and Municipal Hospital, Rochester, New York, 4 cases of constrictive pericarditis were studied by cardiac catheterization. Of these patients, 2 were subsequently treated by pericardiectomy and shown to have chronic fibrosis and inflammation of the pericardium; a third patient died and necropsy revealed chronic constrictive pericarditis with active tuberculosis of the pericardium; in the fourth patient there was radiological evidence of extensive pericardial calcification. All had a high mean right auricular pressure with an M-shaped pattern of pressure curve.

In 3 patients right ventricular pressure curves were obtained and showed the characteristic pattern of slightly elevated systolic pressure followed immediately by a rapid diastolic dip and then by a high diastolic plateau, as described by McKusick (*Bull. Johns Hopk. Hosp.*, 1952, **90**, 3; *Abstracts of World Medicine*, 1952, **11**, 362). The three readings of right ventricular systolic and end-diastolic pressures were 52/18, 35/15, and 36/21 mm. Hg respectively. In the last patient cardiac catheterization 4 months after operation showed that his right ventricular pressure pattern had reverted to normal, the reading having changed from 36/21 mm. Hg preoperatively to 39/8 mm. Hg postoperatively. It is considered that a ratio of right ventricular end-diastolic to systolic pressure greater than 1 to 3 is evidence of chronic constrictive pericarditis and does not occur in other cardio-pulmonary diseases. This ratio is likely to fall below 1 to 3 after successful pericardiectomy. The mechanism of the production of the pressure patterns is discussed.
K. G. Lowe

417. **Intracardial Pressure Curves in Constrictive Pericarditis.** (Courbes de pressions intracardiaques dans la pericardite constrictive)
A. TOURNIAIRE, J. BLUM, F. DEYRIEUX, and M. TARTULIER. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur.*] **46**, 129–142, Feb., 1953. 6 figs., 8 refs.

418. **The Portacaval Shunt Operation, with Special Reference to the Use of Vein Grafts**
P. THERON. *South African Medical Journal* [*S. Afr. med. J.*] **27**, 73–76, Jan. 24, 1953. 5 figs., 7 refs.

In this preliminary paper the author describes 4 cases of cirrhosis of the liver which were successfully treated at the Johannesburg Hospital (University of the Witwatersrand) by a new technique of porta-caval shunt. A side-to-side anastomosis was made between the two vessels, an intervening vein graft forming an H-shaped junction being used. During the anastomosis only a small segment of the portal vein required to be mobilized, thus avoiding a difficult dissection which might have resulted in considerable loss of blood. The two veins were controlled by Southwick clamps, which only partially occluded the vessel, thus permitting a continued blood flow to the liver and reducing the risk of thrombosis. The author points out that an added advantage is that the stoma can be made as large as desired, making it possible in future to use preserved segments of the vena cava rather than autogenous grafts from the superficial femoral vein, as hitherto.

He states that liver failure is the commonest cause of postoperative death in cases of cirrhosis, and emphasizes that all patients should be thoroughly examined in a unit with facilities for studying liver blood flow and portal venography, as well as for the standard liver function tests. Preoperative preparation should include adequate rest in hospital, blood transfusion, and high-protein diet.
A. M. Macarthur

DIAGNOSTIC METHODS

419. **Comparison of Cardiac Output Determined by the Ballistocardiograph (Nickerson Apparatus) and by the Direct Fick Method**
R. T. CATHCART, W. W. FIELD, and D. W. RICHARDS. *Journal of Clinical Investigation* [*J. clin. Invest.*] **32**, 5–14, Jan., 1953. 5 figs., 16 refs.

From comparative determinations made at Columbia University and Bellevue Hospital, New York, on 40 individuals comprising both normal subjects and patients with a variety of clinical conditions, the authors conclude that " the ballistocardiographic measurement of cardiac output gives such erratic results, with so many and such unpredictable errors from case to case, that it should no longer be used in any way whatever as an indication of this function ". *A. I. Suchett-Kaye*

420. **Phonocardiography with Differentiating Filters.** (Herzschallregistrierung mittels differenzierender Filter. Eine Studie zur Herzschallnormung)
H. MAASS and A. WEBER. *Cardiologia* [*Cardiologia (Basel)*] **21**, 773–794, 1952. 10 figs., 16 refs.

In this article from the University Medical Institute, Bad Nauheim, the authors deal with the finer points of phonocardiography. By means of 15 different high-pass filters of various lower-border frequencies, each filter being capable of selecting a particular frequency range, they examined 30 healthy subjects and 52 patients with various cardiac valvular conditions or heart failure. On the basis of their findings they have chosen 6 filters from the 15, and suggest that with these and the help of the electrocardiogram and carotid and venous pulse curves, a complete analysis of various pathological heart sounds and murmurs can be made, and that the use of these 6 filters could lead to a standardized system of phonocardiography. Typical phonocardiograms are reproduced. *G. S. Crockett*

421. **The Q–T Interval in Myocardial Infarction and Left Ventricular Hypertrophy**
S. R. ELEK, A. S. SILVER, J. N. TOBER, and G. C. GRIFFITH. *American Heart Journal* [*Amer. Heart J.*] **45**, 80–85, Jan., 1953. 1 fig., 20 refs.

In 86 cases of acute myocardial infarction studied at the Los Angeles County Hospital (University of Southern California) the Q–T interval in the electrocardiogram was prolonged significantly beyond the upper limit of normal as defined by Ashman, thus confirming the findings of several previous authors, but there was no evidence of a gradual reversion towards normal during the first 6 weeks after infarction. No consistent sex difference was demonstrated. In 120 cases of left ventricular hypertrophy no significant prolongation of the Q–T interval was found, the mean values for " K " (Q–T interval per unit cycle length; QTc) lying well below the upper limit of normal, and all but one lying at or below the mean normal value (Ashman). A semilogarithmic graph in which K values are plotted against the logarithms of cycle lengths is provided, whereby the Q–T formula of Ashman is reduced to a straight line, permitting rapid comparison of observed and predicted Q–T intervals. *William A. R. Thomson*

422. **Anatomic and Electrocardiographic Correlation in Combined Ventricular Hypertrophy**
M. B. LIPSETT and W. J. ZINN. *American Heart Journal* [*Amer. Heart J.*] **45**, 86–94, Jan., 1953. 9 refs.

An analysis is presented of the electrocardiographic patterns in 73 cases from the necropsy records of the Los Angeles County General Hospital between January, 1950, and June, 1951, in which combined ventricular hypertrophy was present (right ventricular wall at least 5 mm., and left ventricular wall at least 14 mm. in thickness) and recent 12-lead electrocardiographic tracings were available. Cases with myocardial infarction, extensive or recent significant pulmonary embolism, bundle-branch block, or with an M-shaped complex in V_1 were excluded. A control group consisted of 17 cases of left ventricular hypertrophy in which the diagnosis of hypertensive heart disease had been made.

It was found that when left ventricular hypertrophy occurred as a result of hypertensive or aortic valvular disease, its electrocardiographic recognition was slightly impaired by the concomitant right ventricular hypertrophy, while in cases in which it was associated with cor pulmonale none of the electrocardiographic criteria of left ventricular hypertrophy was present. The electrocardiographic signs of right ventricular hypertrophy were masked by concomitant left ventricular hypertrophy when it occurred as a result of hypertensive or mitral disease, but not in cases of cor pulmonale. It is concluded that right ventricular hypertrophy in the presence of left ventricular hypertrophy may be suspected when atypical electrical positions are present or the transition zone is shifted to the left. In the only 10 cases in the series in which combined ventricular hypertrophy was diagnosed from the electrocardiogram during life, the presence of right ventricular hypertrophy was recognized from the rotational changes. It is notable that in 14 of the cases none of the criteria of either right or left ventricular hypertrophy was present, enlargement of each ventricle masking the electrocardiographic changes associated with enlargement of the other.
William A. R. Thomson

423. **Intramural Depolarization Potentials in Myocardial Infarction. A Preliminary Report**
M. PRINZMETAL, S. R. KENNAMER, C. MCK. SHAW, N. KIMURA, I. LINDGREN, and A. GOLDMAN. *Circulation* [*Circulation (N.Y.)*] **7**, 1–14, Jan., 1953. 6 figs., 15 refs.

In experiments carried out at the Cedars of Lebanon Hospital (University of California School of Medicine), Los Angeles, on 23 normal dogs, the heart surface was exposed and potentials were recorded from needle electrodes inserted at various depths into the myocardium. All but the terminal millimetre of the electrode was insulated, so that the record was derived mainly from muscle in the immediate vicinity of the tip of the electrode. As the electrode passed into the myocardium from the surface the R wave of the ventricular complex rapidly

diminished, giving way to an rS or QS form at a depth of a few millimetres. Throughout the greater part of the muscle wall a typical " cavity " or QS pattern was thus obtained. Removal of the outer layers of myocardium by cutting or burning caused reduction or loss of the R waves in the epicardial record. Passage of the electrode into and through the interventricular septum confirmed its electrical activation from its left ventricular surface.

In further experiments on 41 dogs myocardial infarction was produced by ligation of the left anterior descending coronary artery. After a variable period of recovery each dog's chest was reopened and intramural potentials were recorded from the infarcted area, the motion of the left ventricle being recorded simultaneously by means of high-speed cinematography in 19 cases. The histology of the relevant portion of the heart was subsequently studied post mortem. In 35 instances there was infarction of the full thickness of the myocardium, and here the epicardial records and intramural records at all depths were identical with the QS pattern obtained from the ventricular cavity. Where some muscle survived in the infarcted area, intramural records again had a QS pattern, with minor differences due to electrical activity in the surviving muscle. In 6 dogs subendocardial muscle necrosis occurred, with normal muscle superficially: epicardial records were then normal. In 7 others extensive subendocardial burns were produced with an electric cautery, and again the epicardial record was normal. A QR pattern was found only when both necrotic and surviving muscle existed on the myocardial surface in the immediate vicinity of the epicardial electrode.

It would appear then that myocardial necrosis is not necessarily associated with the finding of a QR pattern in the epicardial or precordial lead, for a normal surface tracing may be obtained in the presence of extensive necrosis of subendocardial muscle, provided the epicardium is not involved. *J. A. Cosh*

CONGENITAL HEART DISEASE

424. **Asymptomatic Isolated Valvular Pulmonary Stenosis. Diagnosis by Clinical Methods**

S. G. Blount, S. Komesu, and M. C. McCord. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 5–11, Jan. 1, 1953. 4 figs., 13 refs.

In this paper from the University of Colorado School of Medicine, Denver, 6 cases of isolated pulmonary stenosis in children aged 5 to 14 years are reported, and the signs and diagnosis discussed. There was no limitation of activity in any of the patients, who were considered normal by their parents, and they complained of no symptoms.

Discussing the physical signs, the authors point out that on auscultation a systolic thrill and a loud, harsh, grating systolic murmur, usually most intense in the first rather than the second left interspace, are present. The murmur may be transmitted into the vessels of the neck. The second heart sound in this pulmonary area may be normal, of diminished intensity, or absent. The electrocardiogram may be normal or may show hypertrophy of the right ventricle.

Fluoroscopy invariably reveals post-stenotic dilatation of the pulmonary artery. There is marked disproportion between the increased amplitude of pulsation over the main pulmonary artery segment and the normal or decreased amplitude over the right and left pulmonary arteries. The vascularity of the lung field may be normal or slightly decreased towards the periphery. The heart may be normal in size or there may be enlargement of the right ventricle and of the right auricle.

Cardiac catheterization should, in the authors' view, be carried out in all cases to confirm the clinical diagnosis; moreover it is of value in assessing the severity of the condition, a right ventricular systolic pressure of 70 mm. Hg or more indicating the need for operation.

The authors emphasize that this potentially grave congenital abnormality may masquerade as a mild and apparently benign lesion, being often mistaken for a small defect in the auricular or ventricular septum.

T. Semple

425. **Follow-Up Studies on the First 1,000 Patients Operated on for Pulmonary Stenosis or Atresia. Results up to March 1952**

H. B. Taussig and S. R. Bauersfeld. *Cardiologia* [*Cardiologia (Basel)*] **21**, 541–551, 1952; *Annals of Internal Medicine* [*Ann. intern. Med.*] **38**, 1–8, Jan., 1953. 1 ref.

This report is concerned with 1,000 patients who have been treated since November, 1944, by Blalock and his associates by systemic–pulmonary vascular anastomosis, and who have been followed up (except for 6% who could not be traced) for at least 18 months, and in the earliest cases for over 7 years.

" Good " results—defined as marked decrease of cyanosis, rise of arterial oxygen saturation, and subjective improvement—were obtained in 773, and " fair " results —improvement, but with persistent cyanosis and polycythaemia—in 39, while 31 were unimproved; 157 of the patients died at or immediately after operation, an immediate fatality rate of 15·7%.

The majority of the patients (857) were diagnosed before operation as having tetralogy of Fallot; the next most frequent diagnoses were tricuspid atresia (62) and pseudotruncus arteriosus (27). It was later shown that in 40 cases the diagnoses made were incorrect; 29 of these patients died at or shortly after operation. Of 5 patients who were later found to have pulmonary stenosis with an intact ventricular septum, all developed right-sided cardiac failure after their operation; in these cases pulmonary valvotomy would have been a better treatment. Patients with Fallot's tetralogy had the lowest immediate mortality (15%) and the highest proportion of good results (78%), and in addition they developed cardiac failure after operation less often. If cardiac failure is to develop it usually does so within 6 months. In 15 of the patients with Fallot's tetralogy, the aorta over-rode the ventricular septum by more than 50%; all these patients died at operation, or shortly after, from pulmonary congestion. The extent of over-riding cannot be

diagnosed accurately. For all cases of Fallot's tetralogy the delayed mortality was 6%, but for those with a good operational result it was only 4%, and in some of these cases death was not due to the cardiac malformation. The vast majority of patients can adapt themselves to the altered circulation. Those who failed to maintain their improvement (16%) have either died, or have had or are awaiting a second operation, but such operations carry a high fatality rate.

The patients with atypical malformations showed results somewhat less favourable but of the same order; and again the prognosis in those with a good result from operation was notably better than in those with only a fair result. The incidence of subacute bacterial endocarditis was low—22 cases with 4 deaths. Half of these cases occurred within 2 months of operation, confirming the authors' opinion that in the early postoperative period these patients are extremely susceptible to bacterial endocarditis, and it is therefore recommended that large prophylactic doses of penicillin be given. The additional anomaly does not, however, subsequently appear seriously to increase the patients' susceptibility to endocarditis.

[This important article contains detailed statistics and analyses of results.] *M. Meredith Brown*

426. Closure of Atrial Septal Defects with the Aid of Hypothermia; Experimental Accomplishments and the Report of One Successful Case

F. J. Lewis and M. Taufic. *Surgery* [*Surgery*] **33**, 52–59, Jan., 1953. 2 figs., 20 refs.

Marked cooling of the body is associated with a striking reduction in the metabolic rate; during profound hypothermia in the dog it is possible without danger to arrest the flow of blood into the heart long enough to permit an intracardiac operation to be performed under direct vision in a dry field. At the University of Minnesota Medical School the authors applied this principle in the experimental production and closure of atrial septal defects in the dog. Under thiopentone anaesthesia, the animal was cooled by wrapping it in rubberized blankets perfused with cold alcohol solution. The trachea was intubated, and automatic artificial respiration instituted. The rectal temperature fell gradually over a period of 1 to 2 hours from the normal level of 38° C. to 26 or 28° C., and the pulse rate from 150–180 to 50–70 per minute. Right thoracotomy was then performed, the superior and inferior venae cavae occluded with temporary ligatures of heavy silk, and a Satinsky clamp was applied to the base of the heart to occlude the pulmonary artery, aorta, and coronary arteries. The blood flow through the heart was thus arrested for periods up to 8 minutes while, at the first operation, an incision was made in the wall of the right atrium and the greater part of the membranous atrial septum was removed. During closure of the heart the atrium was filled with normal saline to displace all air and obviate the risk of air embolism. At the end of the operation the animal was warmed by running warm alcohol solution through the blankets. At a subsequent operation, the right atrium was opened through the same incision and the defect closed with a continuous silk suture. Saline was introduced into the left atrium by catheter before final closure of the defect, and into the right atrium while the heart was being closed.

Of 39 animals, 27 survived the first operation, 8 of the 12 operative deaths being due to ventricular fibrillation. Of the survivors, 1 died 2 days later with hemiplegia, but the remaining 26 were later subjected to the second operation; there were 8 operative deaths, 4 being due to ventricular fibrillation, and in 1 case the defect was found to have closed spontaneously; the remaining 18 survived the second operation.

Most of the deaths from ventricular fibrillation occurred in early cases, and in the majority this was due to coronary air embolism. In later cases, occlusion of the cardiac outflow by a clamp placed sufficiently low to occlude the coronary arteries was successful in preventing air embolism. Ventricular fibrillation occurred in 7 other cases (2 due to coronary air embolism), in 2 of which the animal recovered after electrical defibrillation, and in the other 5 after cardiac massage.

The same technique has been successfully applied to the closure of an atrial septal defect in a girl of 5 years weighing 29½ lb. (13·4 kg.), and a preliminary case report is given. The patient was anaesthetized with thiopentone and curare and wrapped in the refrigerated blankets until, after 2 hours and 10 minutes, her rectal temperature had fallen to 28° C. (82° F.). Right thoracotomy was then performed and the cardiac blood flow arrested for 5½ minutes while a septal defect 2 cm. in diameter was closed under direct vision. After removing the Satinsky clamp and the ligatures the pulse promptly regained its former strength, and at the end of an operation lasting 58 minutes the rectal temperature was 26° C. (79° F.). The child was warmed by immersion in a warm bath at 45° C. (113° F.) for 35 minutes, by which time her temperature had risen to 36° C. (96·8° F.). Recovery from anaesthesia was prompt and convalescence uneventful. The cardiac murmur disappeared.

F. J. Sambrook Gowar

427. A Method for Surgical Closure of Interauricular Septal Defects

R. E. Gross, E. Watkins, A. A. Pomeranz, and E. I. Goldsmith. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **96**, 1–23, Jan., 1953. 20 figs., 11 refs.

The indications for closure of an atrial septal defect are briefly discussed, and a description of the various operations designed to alleviate this defect is given. The authors then describe in detail their technique, in which the " atrial-well " principle is used to obtain direct access to the interior of the chamber (Gross *et al.*, *New Engl. J. Med.*, 1952, **247**, 455; *Abstracts of World Medicine*, 1953, **13**, 213). Three methods of closure of the atrial defect have been used: (*a*) a Hufnagle double disk button, which engages the edges of the gap; (*b*) suture of a sheet of plastic material to the edges of the defect; (*c*) direct suture of smaller defects.

Details are given of 7 cases in which the operation has been performed. Three patients treated with the button all died, largely because the disks became dislodged

owing to the fact that the rim of the septal defect was not adequately in contact with the disk around its whole circumference. Of the other 4, one was treated by direct suture and did well, the remaining 3 being treated by suture of a nylon membrane over the defect. Of these, one died owing to the formation of a thrombus under a redundant piece of the plastic material, but the other 2 were much improved. *J. R. Belcher*

See also Pathology, Abstract 317

CHRONIC VALVULAR DISEASE

428. **Studies in Mitral Stenosis. IV. The Relative Merits of Various Diagnostic Methods in Mitral Valvular Disease**

G. Biörck, O. Axén, H. Krook, L. Andrén, and H. B. Wulff. *American Heart Journal* [*Amer. Heart J.*] **45**, 13–39, Jan., 1953. 7 figs., 34 refs.

With the introduction of surgical techniques for the relief of mitral disease the differentiation between predominant stenosis and predominant regurgitation has greatly increased in importance, and the authors here re-examine the principles on which that differentiation must be based. In pure mitral stenosis there is distension of the left auricle with a left ventricle of normal size, a typical "stenotic" murmur, an increase in pressure in the left auricle and the pulmonary veins in auricular systole, and a slow circulation through the lungs. In pure mitral regurgitation the left auricle and left ventricle are both enlarged, there is a loud systolic murmur, a systolic pressure wave is found in the left auricle and the pulmonary veins, and although pulmonary circulation is not necessarily delayed, blood may accumulate in the left side of the heart. To distinguish between the two it is necessary therefore to determine the size of the left ventricle, the character of the murmurs, the volume of the left auricle, the changes of pressure in the pulmonary veins, and the way in which the blood passes through the pulmonary circulation and the left heart. The diagnostic methods available include palpation of the apex beat, percussion of the left border of the heart, auscultation, electrocardiography, radioscopy, angiocardiography, electrokymography, and cardiac catheterization with the recording of pulmonary capillary venous (p.c.v.) pressure tracings. Some of these procedures are of limited value: for instance, the interpretation of electrokymograms and p.c.v. tracings is difficult or impossible in the presence of auricular fibrillation; radioscopy is reliable in assessing the size of the left auricle, but less so in the case of the left ventricle; moreover, the significance of enlargement of the left ventricle is difficult to determine when there is also hypertension or a lesion of the aortic valve. The authors have found angiocardiography in the frontal and sagittal planes to be of great help in determining the size of the left auricle and the degree of mitral regurgitation.

At the Almänna Sjukhuset, Malmö, Sweden, the relative value of these various procedures has been tested in 25 cases of mitral disease referred to the authors for possible surgical treatment, the conclusions arrived at by each method concerning the degree of stenosis or regurgitation present being compared with the findings either at operation or at necropsy. In this way the accuracy of the information obtained was assessed, enabling the procedures used to be placed in the following order of diagnostic value: auscultation, radioscopy, angiocardiography and electrokymography, unipolar chest electrocardiogram (ECG), palpation of the apex beat, electrical axis in the standard ECG, and p.c.v. tracings. The ECG was found to give only minor help, signs of right axis deviation indicating some complication but the finding of a normal axis being of no significance.

In 14 cases of mitral stenosis the same procedures, with the exception of angiocardiography, were repeated after operation. The diastolic murmur decreased in intensity but usually without an increase in the systolic murmur, the left auricle commonly became smaller, and the left ventricle enlarged. Cardiac catheterization showed a fall in pressure in the pulmonary circulation.

As the character of the murmurs proved the most helpful diagnostic index, the authors suggest that greater attention be paid to the subject of their evaluation. It is in patients with systolic murmurs of Grades II and III (Levine) that further investigation is necessary to determine whether there is significant mitral regurgitation or not. *Arthur Willcox*

429. **The Selection and Medical Management of Patients with Mitral Stenosis Treated by Mitral Commissurotomy**

G. C. Griffith, H. Miller, R. S. Cosby, D. C. Levinson, S. P. Dimitroff, W. J. Zinn, R. W. Oblath, L. M. Herman, V. J. Johns, B. W. Meyer, and J. C. Jones. *Circulation* [*Circulation (N.Y.)*] **7**, 30–36, Jan., 1953. 1 fig., 5 refs.

Criteria for the selection of patients for mitral valvotomy and a plan of management during the operation period are described. The authors' observations and conclusions are based on a series of 74 cases in which mitral commissurotomy was performed up to May, 1952, at the Los Angeles County Hospital (University of California). There were 8 deaths in the first 35 cases of the series but none in the subsequent 39. (A further 52 operations have been performed since this report, with only one death.)

The criteria for operation are the generally accepted ones. Ideally, the patient should be over 25 and under 40 years of age, without evidence of rheumatic activity, mitral incompetence, or aortic valvular lesion. The left auricle should not be much enlarged and the cardiac rhythm should be normal. Bacterial endocarditis should be excluded. Congestive failure which is more than temporary and reversible is a contraindication. The authors state that a pulmonary arterial pressure which is moderately increased falls satisfactorily after operation, with a good clinical result; but a greatly increased pressure is often associated with cardiac enlargement, auricular fibrillation, or chronic congestive failure, and is considered a contraindication to operation. They regard

a history of recent systemic embolism as an indication for operation, amputation of the left auricular appendix and an improved cardiac output lessening the risk of thrombosis within the auricle and of further embolism.

During the operation rapid auricular fibrillation is controlled with ouabain and ventricular extrasystoles with procainamide, both given intravenously. A long-acting heparin is given by intramuscular injection periodically in the immediate postoperative period if clots are found in the auricle. No attempt is made to convert auricular fibrillation to normal rhythm until one or two months after operation *J. A. Cosh*

430. An Interpretation of the Incidence of Mural Thrombi in the Left Auricle and Appendage, with Particular Reference to Mitral Commissurotomy

J. B. WALLACH, L. LUKASH, and A. A. ANGRIST. *American Heart Journal* [*Amer. Heart J.*] **45**, 252–254, Feb., 1953. 7 refs.

431. Interrelationships among Pulmonary " Capillary " Pressure, Blood Flow and Valve Size in Mitral Stenosis. The Limited Regulatory Effects of the Pulmonary Vascular Resistance

J. ARAUJO and D. S. LUKAS. *Journal of Clinical Investigation* [*J. clin. Invest.*] **31**, 1082–1088, Dec., 1952. 2 figs., 18 refs.

At the New York Hospital–Cornell Medical Center, New York, 36 cases of mitral stenosis of varying severity were studied by means of cardiac catheterization, 0·2 g. of amylobarbitone being given before the start of each investigation. The pulmonary " capillary ", pulmonary arterial, and right ventricular pressures and the cardiac output were estimated at rest and again during the last 2 minutes of a 5-minute exercise period. The area of the orifice of the mitral valve (M.V.A.) was estimated by the method of Gorlin and Gorlin, and was expressed as an index related to surface area, the pulmonary " capillary " (P.C.) pressure was taken as that of the pulmonary veins or left atrium, and the pulmonary vascular resistance (P.V.R.) was calculated by means of Apéria's formula.

To maintain the blood flow across the stenotic mitral valve an increase in left atrial, pulmonary venous, and P.C. pressure takes place. At rest the P.C. pressure was found to remain within the range of the osmotic pressure of the plasma, owing to the fact that the resting cardiac output varied directly with the size of the mitral orifice. The mode of regulation of the cardiac output is unknown, but it evidently does not depend on the pulmonary vascular resistance, as this value varied independently of the size of the mitral orifice. An increased P.V.R. did not prevent a great increase in P.C. pressure on exercise, but although the P.C. pressure surpassed the osmotic pressure in every case, acute pulmonary oedema occurred in only one subject. It is concluded that changes in the permeability of the alveolar membrane protect the subject against oedema. The increased P.V.R. may be the result of anatomical changes, as there exists a close correlation between this value and the degree of vascular sclerosis in the lungs.

A. T. Macqueen

HEART FAILURE

432. Neurohemodynamics of Pulmonary Edema. III. Estimated Changes in Pulmonary Blood Volume Accompanying Systemic Vasoconstriction and Vasodilation

S. J. SARNOFF, E. BERGLUND, and L. C. SARNOFF. *Journal of Applied Physiology* [*J. appl. Physiol.*] **5**, 367–374, Jan., 1953. 3 figs., 26 refs.

Working at the Harvard School of Public Health, Boston, the authors have shown that the intracisternal injection of fibrin in dogs produces marked vasoconstriction in the systemic arterial bed, and that this is accompanied by a rise in arterial pressure and in left auricular pressure and an increase in lung weight. The latter was measured *in vivo* by a new suspension method which is described. These changes could be reversed when " Ro 2-2222 " (" arfonad "), a ganglionic blocking agent, was injected intravenously, causing peripheral vasodilatation. The pressure–volume curve of the pulmonary vascular bed *in vivo*, which was also determined, was found to conform with curves obtained from isolated lung preparations.

In their discussion the authors argue that the increase in lung weight must be due to a shift of blood from the systemic to the pulmonary vascular bed. It appears that the pulmonary vascular bed behaves passively, its volume depending on the changes in the volume of the systemic circulation. *J. Naish*

433. The Use of 2-Ethylhexanol in Acute Pulmonary Edema

N. E. REICH, B. A. ROSENBERG, and M. METZ. *Diseases of the Chest* [*Dis. Chest*] **23**, 43–49, Jan., 1953. 1 fig., 15 refs.

Since a large amount of fluid in the respiratory passages can be tolerated provided no foam is formed, the inhalation of anti-foaming agents has been suggested as an adjunct to the measures usually employed in the treatment of acute pulmonary oedema. The present authors have employed for this purpose 2-ethylhexanol (octyl alcohol), which is non-toxic, volatile, and easily available, being widely used in industry. It is administered by passing oxygen at a rate of 9 litres per hour through a humidifier charged with a mixture of 2 parts of water and one part of 2-ethylhexanol, the patient inhaling the vapour through a B.L.B. mask.

This method was used in the treatment of 14 cases of severe acute pulmonary oedema, most of them due to hypertensive, ischaemic, or rheumatic heart disease, at Kings County Hospital, Brooklyn, New York. Other necessary treatment was given only after the effect of the inhalation had been observed on the respiratory rate, heart rate and rhythm, blood pressure, occurrence and severity of cough, cyanosis, and apprehension, and the " extent of pulmonary moisture ", the time taken for appreciable clinical improvement to appear being noted. All but 3 patients are said to have obtained some benefit from the treatment, while 5 patients showed marked improvement within 15 minutes. Three illustrative case histories are given. Further studies are in progress

using undiluted 2-ethylhexanol with oxygen under intermittent positive pressure, and the results are said to be encouraging.

[The authors are to be congratulated on their ingenuity, but their appraisal of the results leaves out of account the effects of rest and posture and of the oxygen which was used as a vehicle. Moreover, the information they give about the causal condition, the duration of oedema before treatment, and the history of previous attacks in each case is tabulated in such a way that the reader cannot correlate these factors with the degree of relief obtained. Since it is not claimed that any major benefit is to be expected from this form of treatment, which is intended as an adjuvant only, conditions suitable for the exact evaluation of results would in any case be very difficult to obtain.] *Bernard Isaacs*

434. **The Effect of Posture on the Excretion of Water and Sodium by Patients with Congestive Heart Failure**
T. A. LOMBARDO. *Circulation* [*Circulation* (*N.Y.*)] **7**, 91–95, Jan., 1953. 1 fig., 11 refs.

At the Medical College of Alabama, Birmingham, Alabama, 4 patients with congestive heart failure were studied in both the sitting and the recumbent positions for 9-hour periods during which they ingested 200 ml. of a 0·14% solution of sodium chloride every 30 minutes. In both positions they showed a delayed and inadequate diuresis. Water was retained in excess of salt, leading to hyponatraemia with raised venous pressure, reduced vital capacity, and prolonged circulation time. The fact that the patients did not give the normal response (that is, increased sodium excretion in the recumbent posture) is interpreted by the author as yet another indication that his previously postulated intracranial volume-regulating centre does not operate in the presence of congestive cardiac failure. *K. G. Lowe*

CORONARY DISEASE AND MYOCARDIAL INFARCTION

435. **Diagnostic and Therapeutic Value of the Reproduction of Chest Pain**
T. J. REEVES and T. R. HARRISON. *Archives of Internal Medicine* [*Arch. intern. Med.*] **91**, 8–25, Jan., 1953. 4 figs., 5 refs.

A pain in the chest is often related by the patient to serious heart disease, and it is therefore of great importance to determine whether the pain is due to angina pectoris or to some other condition. With this end in view the authors, who studied this problem at the Medical School, Birmingham, Alabama, discuss simple tests which may help to differentiate the various causes of pain. The tests entail reproduction of the pain and are carried out, so far as is possible, under conditions prevailing at the time of spontaneous attacks—as, for example, after meals or in a cold atmosphere. They include the taking of electrocardiograms before and after exercise sufficient to cause pain; assessing the effect of glyceryl trinitrate in inhibiting attacks; and the provocation of skeletal or gastro-intestinal pains by pressure on the chest walls, special movements, and inflation of the stomach or colon with air. Naturally, in very ill patients the objective findings are usually enough for a diagnosis. Patients with chest pain are most often ambulatory, and clinical, cardiographic, and radiological studies may fail to yield positive information as to the cause of the pain. It is in this group of cases, in which objective findings are lacking, that the diagnosis may at times be established by procedures which reproduce the pain.

The authors conclude that the diagnosis of angina pectoris is doubtful unless two criteria are satisfied: (1) the pain should be reproducible by exertion under appropriate conditions as regards meals, cold, or emotional stress; and (2) it should be shown that the same physical effort under the same conditions does not cause pain if undertaken a few minutes after the administration of glyceryl trinitrate. *James W. Brown*

436. **The Treatment of Angina Pectoris with Khellin. Part II**
J. J. CONN, R. W. KISSANE, R. A. KOON, and T. E. CLARK. *Annals of Internal Medicine* [*Ann. intern. Med.*] **38**, 23–27, Jan., 1953. 4 refs.

In a previous paper (*Ann. intern. Med.*, 1952, **36**, 1173; *Abstracts of World Medicine*, 1952, **12**, 420) the authors described the results obtained with khellin (" ammivin ") in the treatment of 42 patients with angina pectoris. In the present paper they report the results obtained in a second series of 42 patients with angina, the form of khellin used being known as " khelloyd ". The drug was given by mouth (supplemented in a few cases by parenteral injection) in a dose of 25 mg. daily for the first week, increased at weekly intervals by 25 mg. a day until a therapeutic response or a reaction was obtained. The highest dose was 100 mg. daily. In 12 patients treatment had to be abandoned because of nausea or vomiting. Of the 42 patients 14 did not benefit from treatment, 2 responded unfavourably, one died from acute myocardial infarction during treatment, and the remainder (25) showed some benefit in the form of a decrease in the number and severity of the attacks. Some response was obtained in patients with old myocardial infarction, but no benefit was observed in patients with acute myocardial infarction.

The authors conclude that khellin is of value in the treatment of angina but will not replace other vasodilator drugs unless the incidence of side-effects can be reduced. *J. McMichael*

437. **Khellin in the Treatment of Angina Pectoris**
R. HILL and A. G. MELROSE. *Glasgow Medical Journal* [*Glasg. med. J.*] **34**, 17–21, Jan., 1953. 16 refs.

438. **Length of Survival After Myocardial Infarction**
C. SMITH. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 167–170, Jan. 17, 1953. 12 refs.

In 1942 the author and his colleagues published the results of a 10-year follow-up of 100 consecutive patients with coronary thrombosis (*Ann. intern. Med.*, **17**, 681), 66 of the patients being alive at the time of the report. In the present paper the author reports his findings

in the same series of cases after a further 10-year period. At the beginning of 1952, 16 of the original 100 patients were alive, 69 were known to be dead, and 15 were lost to follow-up.

The author states that according to the literature the average duration of life after myocardial infarction is 41·1 months; in his series 60 patients lived longer than this. Of the 35 patients who died between 1941 and 1952, 14 lived well into the second decade after the initial attack. No definite relation was observed between the age of the patient at onset and the survival time. Co-existing hypertension appeared to influence the survival time, as did recurrent attacks of myocardial infarction. Of 30 patients followed up for more than 10 years, 14 had hypertension before the onset of myocardial infarction, and 9 of these died; 13 of the 30 had a second or third attack of myocardial infarction and 9 of these 13 died. In cases in which there were persistent changes in the electrocardiogram the prognosis was poor. Cerebral vascular complications were common. No case of neoplastic disease was encountered in the series.

C. W. C. Bain

439. **The Urinary Output of Catechol Derivatives Including Adrenaline in Normal Individuals, in Essential Hypertension, and in Myocardial Infarction**
F. R. NUZUM and F. BISCHOFF. *Circulation* [*Circulation (N.Y.)*] **7**, 96–101, Jan., 1953. 17 refs.

In view of past disappointment with their attempts to measure adrenaline levels in the blood, the authors set out to confirm the findings of Kroneberg and Schümann (*Arch. exp. Path. Pharmak.*, 1950, **209**, 350) that there is an increase in the conjugated pyrocatechol fraction (liberated by acid hydrolysis and related to noradrenaline) in the urine of hypertensive patients. In this investigation, using the microcolorimetric method described by Shaw (*Biochem. J.*, 1938, **32**, 19), which depends on the catalytic reduction of arsenomolybdic acid to a blue-coloured compound by adrenaline-like substances, they studied the catechol fractions of the urine in 17 normal individuals, 17 patients with well-established essential hypertension, and 8 patients with ischaemic heart disease (4 with severe angina pectoris and 4 recovering from myocardial infarction) within the age range 45 to 68 years, at the Cottage Hospital Research Institute, Santa Barbara, California. The urine was pre-treated with alkali (which increases the final colour due to adrenaline fivefold but does not effect that due to noradrenaline and like substances) in that part of the estimation devoted to urinary adrenaline content. The method is described in detail.

The ratio of catechol derivatives in hydrolysed and unhydrolysed urine of normal subjects found by the authors agreed well with the findings of Kroneberg and Schümann, but they could not confirm that in hypertensive patients there is a marked rise in this ratio, although it was observed in 3 patients with myocardial infarction. Adrenaline was found in the urine of some patients in all of the three categories examined, and was present in considerable amount in 2 patients with myocardial infarction.

K. G. Lowe

HYPERTENSION

440. **Sinoaortic Regulatory System. Role in Pathogenesis of Essential and Malignant Hypertension**
P. KEZDI. *Archives of Internal Medicine* [*Arch. intern. Med.*] **91**, 26–34, Jan., 1953. 3 figs., 19 refs.

In this paper from the Wesley Memorial Hospital, Chicago, some of the theories of hypertension, together with work on carotid-sinus block in normotensive and hypertensive subjects, are reviewed. The author concludes that there is no disruption of the carotid-sinus receptors in either essential or malignant hypertension, and that these act normally at any pressure level. Stimulation of the carotid sinus depends on the elasticity of the carotid arterial wall, and this elasticity is reduced in hypertension.

The receptors of the carotid sinus perceive the elevated blood pressure in hypertension as being normal because the raised blood pressure of hypertensive patients causes only the same degree of pulsatile expansion of the less elastic arterial walls and the same amount of stimulation to the carotid-sinus receptors as does a normal blood pressure in normotensive subjects.

James W. Brown

441. **The Relationship of Retinal and Renal Arteriosclerosis in Living Patients with Essential Hypertension**
J. P. WENDLAND. *American Journal of Ophthalmology* [*Amer. J. Ophthal.*] **35**, 1748–1752, Dec., 1953. 1 fig., 23 refs.

In an investigation carried out at the University of Minnesota Medical School on 80 patients suffering from essential hypertension the degree of sclerosis present in the smaller renal vessels, as estimated histologically (using Bell's grading) in biopsy material obtained during sympathectomy, was compared with that in the retinal arteries, as judged ophthalmoscopically according to the classification of the American Ophthalmological Society.

A fairly high degree of correlation was found between the two organs, the degree of arteriolosclerosis being placed in the same or neighbouring grades in 86% of the cases. There was, however, a definite tendency for retinal arteriolosclerosis to be more advanced than renal, and in 19 cases there was no sclerotic change in the kidney vessels although it was present in the retina. This suggests that the renal arteriolosclerotic changes in essential hypertension are secondary to the hypertension, or due to an independent process which is enhanced by it.

J. E. M. Ayoub

442. **Dietary Treatment of Hypertension**
I. H. PAGE and A. C. CORCORAN. *Journal of Clinical Nutrition* [*J. clin. Nutrit.*] **1**, 7–16, Sept.–Oct., 1952. 3 figs., 21 refs.

The authors, writing from Cleveland, Ohio, briefly review the history and experimental basis of treatment of hypertension by restriction of sodium in the diet. They point out that experimental work regarding the relation between vascular reactivity and sodium retention has

been confused by species differences. It is their opinion that in the clinical evaluation of dietary treatment of hypertension in human beings it is essential to have a preliminary control period, during which repeated blood-pressure determinations are made, with the aim of achieving a stabilized state while the patient is on a relatively constant, normal intake of sodium and protein. Some patients may reach this condition in a few weeks, whereas in others it may take some months. During part of this time the diet should contain 0·2 g. sodium with added salt in enteric-coated tablets. Sodium restriction can be started by replacing these by a placebo in tablets of identical appearance. Estimations of urinary sodium concentration are made throughout the study. Sodium intake should be increased to a normal level for a further control period after the test.

It was found that under these conditions a minority of hypertensive patients respond to sodium restriction by fall in blood pressure and improvement in the pattern of hypertensive vascular disease. Similar studies with the rice diet of Kempner showed that its efficacy is related only to its low sodium content. It is not considered possible to forecast which cases will respond to sodium restriction, nor is it common to get a speedy answer to the question during the period when the patient is receiving the diet, even when, in addition to sodium restriction, mercurial diuretics are given, as the beneficial action of the diet may be long delayed. Many social, economic, and personal factors were found to militate against successful adherence to the diet; there is, moreover, in the presence of moderate or severe renal failure, the danger of sodium depletion.

The authors conclude that the practical choice lies between rice diet and other diets of low sodium content (less than 200 mg. per day). Extradietary sources of sodium (stomach powders, water-softeners) should be avoided; salt substitutes are unsatisfactory and, in the case of lithium chloride, dangerous. Cation-exchange resins are less satisfactory in the treatment of hypertension than in that of congestive heart failure or nephrotic syndrome. Low-sodium diet can with advantage be combined with hexamethonium therapy. In malignant hypertension speedier measures than sodium restriction are, as a rule, needed. *K. G. Lowe*

443. **1-Hydrazinophthalazine (Apresoline) in the Treatment of Hypertension: a Two Year Study**
J. H. HAFKENSCHIEL and M. A. LINDAUER. *Circulation* [*Circulation (N.Y.)*] **7**, 52–57, Jan., 1953. 2 figs., 20 refs.

At the Hospital of the University of Pennsylvania, Philadelphia, 40 hypertensive patients have been observed for 1 year or longer while on a low-salt diet and receiving 1-hydrazinophthalazine (" apresoline ") in a dosage of up to 200 mg. by mouth 4 times a day. Of 33 patients who were considered to belong to Smithwick's Groups I to III in regard to expectation of life, 19 were considered to show a satisfactory lowering of blood pressure, but this occurred in only 1 out of 7 patients belonging to Smithwick's Group IV. In 6 patients who were given placebos in place of the drug the blood pressure rose again. When administration of the drug was resumed it was noted that there was an undue susceptibility to it, and the authors recommend that resumption should be with small, increasing doses. During prolonged administration there was little alteration in tolerance to the drug.

Side-effects occurred early in treatment, the most frequent being headache, palpitation, nausea, and vomiting. Toxic cumulative effects were not evident. The one death (due to myocardial infarction) in this series appeared to be unrelated to therapy. There was no evidence of improvement in renal function or reduction in heart size, although 3 patients showed an improvement in the electrocardiogram; 4 patients showed improvement of retinopathy, in 30 there was no change, and in 6 there was deterioration. The authors consider that the period of observation was too short to judge whether the drug had any favourable effect on the natural history of hypertensive vascular disease.

K. G. Lowe

444. **The Use of *Rauwolfia serpentina* in Hypertensive Patients**
R. W. WILKINS and W. E. JUDSON. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 48–53, Jan. 8, 1953. 6 refs.

Extract of *Rauwolfia serpentina* has long been used in India in the treatment of a variety of conditions, and is reported to have a sedative and hypotensive effect. A clinical trial of the drug, in the form of " serpina " tablets, has been carried out at the Evans Memorial Hospital (Boston University School of Medicine) on 59 patients suffering from hypertension, which was usually diagnosed as " essential ", but in a few cases as " renal ". After a period of observation of " at least several weeks ", with or without other hypotensive drugs, treatment was started with 1 to 4 tablets [weight not stated] of serpina daily by mouth. In contrast to the procedure usually adopted in India, the drug was given in continuous rather than interrupted courses. A total of 39 cases were treated with serpina alone: if the blood pressure fell to 150/99 mm. Hg within 6 to 10 weeks a placebo was sometimes substituted, but no other drug was added; but if the blood pressure remained above that level, either veratrum viride (as " veriloid ") in the maximum dosage which could be tolerated (8 to 20 mg. daily) or hydrazinophthalazine in doses gradually increasing from 50 to 800 mg. a day was given in addition. In the remaining cases serpina was given in addition to veriloid or other drugs.

In the 39 cases treated with serpina tablets alone the average blood pressure fell from 192/112 to 165/95 mm. Hg, and the pulse rate from 82 to 72 per minute. This compares favourably with a reduction of blood pressure from an average of 196/115 mm. Hg to 186/111 mm. Hg in 27 patients given only placebos. On cessation of therapy, or on substitution of a placebo, the blood pressure rose again, but not immediately, taking up to a month to reach its original level. Several patients who had responded only moderately to the maximum tolerated dose of veratrum viride showed a further decrease in blood pressure when serpina was given in

addition, and a similar additive action was noted with hydrazinophthalazine, while it was found that the palpitations and headache caused by this last drug were alleviated by serpina. When patients failed to respond adequately to a combination of two of the drugs, the third was added, often with further reduction of blood pressure. In 18 such patients the blood pressure was reduced from an average of 195/117 mm. Hg during the control period to 144/82 mm. Hg during treatment with all three drugs.

Symptomatic improvement was often dramatic. A sense of relaxed well-being, decreased irritability, improvement in personality, and relief of headache, fatigue, and dyspnoea were frequently described. A carefully controlled experiment indicated that this symptomatic improvement was real and it was perhaps the most easily identified effect of the drug. No serious side-effects were noted, though nasal congestion was frequent, suggesting that the drug dilates the blood vessels of the nasal mucous membrane; extraordinary dreams and nightmares were noted by some patients. Bradycardia occurred frequently, but postural hypotension was not observed. The sedative effect of the drug was confirmed, and may in some cases make it necessary to limit the dosage.

On the whole, the authors were favourably impressed, and are of the opinion that serpina may prove to be a valuable hypotensive drug, particularly in combination with veratrum viride and other substances. Further study is recommended. *Robert Hodgkinson*

445. **The Surgical Creation of an Arterio-venous Fistula with Proximal Ligation of the Vein in the Treatment of Severe Hypertension.** (Réalisation chirurgicale d'une fistule artério-veineuse avec ligature veineuse sus-jacente dans le traitement de la grande hypertension artérielle permanente)

C. LIAN. *Cardiologia* [*Cardiologia (Basel)*] **21**, 346–352, 1952. 8 refs.

The author discusses in a general way the treatment of hypertension by the creation of an arterio-venous fistula, with reference to 17 cases in which this procedure was carried out by Welli at the Hôpital de la Pitié, Paris. An arterio-venous fistula caused by trauma may lead in some cases to heart failure, but it seldom does so until many years after its establishment. However, in 5 of 7 hypertensive patients in whom an artificial fistula between the femoral artery and vein was established, cardiac insufficiency developed within a few months. For this reason, in the next 8 patients the anastomosis was combined with ligation of the femoral vein immediately above it so as to avoid reflux of blood towards the right heart; only one of these patients developed cardiac failure, some 2 months later, and eventually died with ventricular fibrillation. A further 2 patients were treated by anastomosis of the axillary artery and vein, in one case with proximal venous ligation.

The average fall in blood pressure resulting in the 17 patients was 30 mm. Hg systolic and 20 mm. Hg diastolic. The operation was carried out under local analgesia, the femoral vessels being exposed about the middle of the thigh. Potts clamps were applied to both vessels, in which incisions 5 or 6 mm. long were then made. The vein was ligated above the anastomosis, but not too close to it, and preferably above the first collateral branch. No anticoagulants were employed, and there were no operative deaths.

The operation is recommended for patients whose diastolic blood pressure is 140 mm. Hg or more, or for those with a pressure of over 120 mm. Hg whose symptoms are severe. Contraindications to the operation are heart failure, renal failure, age over 60, and a poor general condition.

[Except for mention of the patient who died no follow-up results are given.] *M. Meredith Brown*

446. **Nephrectomy and Other Treatment for Hypertension in Pyelonephritis**

G. W. PICKERING and R. H. HEPTINSTALL. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **22**, 1–22, Jan., 1953. 6 figs., 32 refs.

The results of excision of one diseased kidney for the relief of hypertension in 12 patients treated during the last 11 years at St. Mary's Hospital, London, are reported and the aetiology, pathology, and clinical features of chronic atrophic pyelonephritis—the lesion most commonly found in the excised kidney—are reviewed, the typical morbid changes being illustrated by one photograph and 5 photomicrographs.

Nephrectomy brought about considerable and persistent reduction of blood pressure in 4 of these 12 patients. It was ineffective in one patient whose excised kidney proved to be tuberculous, in 4 with bilateral pyelonephritis (although one of these died on the 10th postoperative day from pulmonary embolism), and in 3 in whom the condition was believed to be unilateral (although proof of this was obtained post mortem in only one of these). Subtotal adrenalectomy afforded relief in 2 children whose hypertension had entered the malignant phase, nephrectomy having failed, and an additional case, not included in the series, is described in which subtotal adrenalectomy and subdiaphragmatic sympathectomy (without nephrectomy) relieved malignant hypertension associated with bilateral pyelonephritis. In none of the 7 cases in which hypertension was reduced by nephrectomy or adrenalectomy or both, however, did the blood pressure fall to within normal limits during periods of observation which extended up to 10 years.

There are four possible explanations for the failure of nephrectomy to relieve hypertension in cases of apparently unilateral kidney disease: (1) hypertension of more than about 2 years' duration may have become irreversible; (2) it may have entered the malignant phase; (3) it may not have been the consequence of the renal lesion; or (4) undetected pyelonephritis may have been present in the other kidney. From the findings in this series and others reported in the literature the authors conclude that unsuspected bilateral disease is the commonest reason for failure. Hence if the condition is known to be bilateral, excision of the more severely affected kidney is unlikely to do good, and may do harm. On the other hand if hypertensive neuroretinopathy (albuminuric

retinitis) is present, urgent measures for the relief of the hypertension are required, such as: (1) subtotal adrenalectomy, which proved successful in the 3 cases reported here, but failed in 3 other cases in adults whose malignant hypertension was not the result of pyelonephritis; (2) sympathectomy, which was not adequately investigated in the present series; and (3) the parenteral administration of hexamethonium compounds.

Adrian V. Adams

BLOOD VESSELS

447. **The Ankle Blow-out Syndrome—a New Approach to the Varicose Ulcer Problem**

F. B. COCKETT and D. E. E. JONES. *Lancet* [*Lancet*] **1**, 17–23, Jan. 3, 1953. 14 figs., 20 refs.

Ulcers of the lower third of the leg may be infective, traumatic, or associated with arteriosclerosis or erythrocyanosis, or they may belong to the group which, for want of a better term, are called varicose ulcers. In the authors' opinion this name is unfortunate because the condition often appears to be a separate disease, bearing no relation to varicose veins, as is shown by the following points: (1) many patients with ulcers show no evidence of saphenous valvular incompetence; (2) many patients with long-standing incompetence of the saphenous veins have no ulcers; and (3) efficient treatment of the varicose veins fails to cure the ulcers in a high proportion of cases in which the two occur together.

Moreover, a local cause is suggested by certain facts: (1) these ulcers have a constant anatomical position just behind and above the malleolus, usually the internal; (2) efficient pressure on the ulcer usually induces it to heal, even in ambulant patients; and (3) in many cases the ulcer is associated with previous thrombosis of the deep veins. This possibility was therefore investigated by the authors at St. Thomas's Hospital, London.

Clinical observation showed that the earliest change found before ulceration develops is a local venous dilatation which is not necessarily associated with saphenous incompetence. Anatomical studies showed that the venous drainage of the subcutaneous tissues in the ulcer-bearing area is not into the saphenous vein, but directly into the deep veins of the calf through three easily definable perforating veins, constant in position, each of which has a valve near its junction with the deep vein. These veins being situated below the muscle pump of the calf, it follows that incompetence of their valves will throw a great strain on the venous mesh which they drain, resulting in dilatation and stagnation of venous blood in the ulcer-bearing area. Similarly, if thrombosis of the deep veins occurs, the perforating veins may provide an alternative path for the return of blood, the valves first having been destroyed, with the same result.

This theory of the mechanism of ulceration of the lower leg, for which the name " ankle blow-out syndrome " is suggested, has been confirmed by the finding of incompetent and dilated perforating veins at operation in a number of cases, and the authors describe their technique of tying such vessels. It is pointed out that the theory provides an explanation of many puzzling points, particularly the effect of local pressure, and the frequent lack of effect of saphenous ligation, on this type of ulcer.

[This article is an original contribution of considerable practical value. In the abstracter's opinion it will do a great deal to clear up confusion in this field and to place treatment on a sound practical footing.] *C. G. Rob*

448. **Ligation of the Popliteal Vein for the Gravitational Syndrome**

H. D. MOORE. *Lancet* [*Lancet*] **1**, 23–25, Jan. 3, 1953. 8 refs.

The author reviews his experience in the treatment of the gravitational syndrome by ligation of the popliteal vein in 23 cases (18 patients). Only those patients were treated in whom no valves could be demonstrated in the deep veins by ascending phlebography.

Of 13 legs in which ulceration was the primary complaint, 9 healed after operation and have remained so for an average period of just under 2 years, another broke down again after remaining healed for 2 years and 2 months, while 4 ulcers failed to heal but were no worse after the operation. The author emphasizes that the ulcer must be allowed to heal before the patient is discharged from hospital.

Of 5 patients (7 legs) in whom pain and discomfort were predominant but who had no ulceration, all were relieved; and of 2 patients (3 legs), also without ulceration, whose chief complaint was swelling, one was relieved in both legs, and the other has been treated only recently. *C. G. Rob*

449. **Granuloma of the Nose and Periarteritis Nodosa**

H. J. M. STRATTON, T. M. L. PRICE, and M. O. SKELTON. *British Medical Journal* [*Brit. med. J.*] **1**, 127–130, Jan. 17, 1953. 2 figs., 15 refs.

The authors report 2 cases in which a patient was admitted to St. Nicholas Hospital, Plumstead, with severe nasal sepsis and swelling due to a chronic ulcerating granulomatous infection and died of generalized periarteritis nodosa within 6 months. The histological appearances on biopsy of the nasal mucosa in the first case led to a diagnosis of " giant-cell granuloma of nasal sinuses " and a tentative diagnosis of periarteritis nodosa, which was later proved to be correct. In the second case sinus infection preceded by 3 months the development of a granulomatous ulcer on the septum, the macroscopical and histological appearances of which were similar to those in the first case. Death occurred later from periarteritis nodosa.

The authors review the scanty literature on this subject. Assuming that " malignant granuloma of the nose " (Woods, *Brit. med. J.*, 1921, **2**, 65) might be a variant of the syndrome, they obtained histological specimens from 4 cases of the latter disease, but were unable to find evidence of periarteritis. Nonetheless, in several cases of malignant granuloma of the nose reported in the literature the patient died later from periarteritis nodosa. The question whether the nasal infection is the cause of, or merely a lesion due to, periarteritis nodosa is discussed. *J. Naish*

Haematology

450. **The Use of Cobaltous Chloride in the Anemia Associated with Chronic Renal Disease**
F. H. GARDNER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **41**, 56–64, Jan., 1953. 3 figs., 19 refs.

The part played by cobalt in erythropoiesis is still undetermined, some authors regarding it as a non-specific erythropoietic stimulant, and others as a specific nutritional component required for the production of haemoglobin or erythrocytes. In the present paper from the Peter Bent Brigham Hospital, Boston, the author describes the effect of the administration by mouth of cobaltous chloride for 4 weeks or longer to 17 patients with renal disease and anaemia. During treatment there was a rise in the erythrocyte count, haemoglobin level, and haematocrit values; no other changes in the peripheral blood were seen. This rise was associated with an increased sense of well-being, but no apparent change in the course of the underlying renal disease. If the drug was discontinued, the blood constituents returned to pre-treatment levels.

The author discusses the possible toxic complications from the use of cobalt; for instance, 4 patients in his small series developed some lesion of the 8th cranial nerve, with tinnitus in all 4 and severe deafness in one case [but further details are not given]. He concludes the drug should be used only with full recognition of the possible toxic complications. *Janet Vaughan*

451. **Optic Nerve Degeneration in Pernicious Anaemia**
H. H. HYLAND and V. J. H. SHARPE. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **67**, 660–665, Dec., 1952. 4 figs., 7 refs.

While it has long been known that visual impairment occurs in pernicious anaemia owing to retinal haemorrhage or thrombosis of retinal vessels, it is less well known that there may be involvement of the optic nerves, causing progressive visual impairment and ultimate atrophy. The literature contains reports of 26 cases of optic-nerve involvement in pernicious anaemia, and the present authors add 4 more. The chief feature was a centrocaecal scotoma, and the chief symptom was visual failure. The authors state that if the visual impairment is the initial and dominant symptom, a diagnosis of pernicious anaemia may not be suspected. Again, if visual impairment is associated with spinal-cord involvement, disseminated sclerosis or tabes dorsalis may be diagnosed.

In the authors' series vision improved with adequate liver therapy in cases without marked atrophy. In one case vision improved although symptoms had been present for 6 months to a year. The authors consider that in every middle-aged patient with progressive loss of vision pernicious anaemia should be looked for, even if there is a history of excessive smoking. If the results of blood examination suggest pernicious anaemia and there is no free hydrochloric acid on gastric analysis, a therapeutic trial of liver therapy is indicated.
C. McCulloch

452. **Maintenance Therapy of Pernicious Anemia with Vitamin B_{12}**
G. C. MEACHAM and R. W. HEINLE. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **41**, 65–77, Jan., 1953. 1 fig., 10 refs.

From the Western Reserve University School of Medicine and Hospital, Cleveland, Ohio, the authors report the results of a controlled study of maintenance treatment with vitamin B_{12} in 43 cases of pernicious anaemia. Patients were given crystalline vitamin B_{12} or a concentrate containing vitamins B_{12} and B_{12b}, that is, cyanocobalamin and hydroxocobalamin. In the doses used, these substances were as effective as purified liver extract. An average daily dose of 1 μg. given intramuscularly at intervals of 3 to 4 weeks appeared adequate to maintain normal erythrocyte levels and to prevent the appearance of neurological or lingual lesions. Mild macrocytosis, however, persisted in many patients, and was not affected by the addition of either folic acid or purified liver extract. The authors suggest that possibly some other, so far unrecognized, factor or factors may be necessary to redress completely the erythrocytic abnormality of pernicious anaemia.
Janet Vaughan

453. **The Treatment of Pernicious Anemia with Massive Parenteral Doses of Vitamin B_{12}**
E. H. REISNER and L. WEINER. *Blood* [*Blood*] **8**, 81–85, Jan., 1953. 17 refs.

The authors have studied the effect of massive doses of vitamin B_{12} (cyanocobalamin) in patients in Bellevue Hospital, New York, suffering from pernicious anaemia in relapse, and also in stabilized cases with subacute combined degeneration of the cord.

In 14 patients with proven pernicious anaemia in relapse treated with a single intramuscular dose of 1,000 μg. of crystalline vitamin B_{12}, a complete haematological remission resulted in all but 1 case. In 9 patients the duration of the remission ranged from 3 to 7 months while in 4 patients later lost from the follow-up no relapse had occurred when last seen 4, 6, 8, and 9 months respectively after treatment. In 2 patients the erythrocyte count was over 6,000,000 per c.mm., and it is thought that one of these may have developed a true polycythaemia. The 7 patients suffering from subacute combined degeneration of the cord (who had shown no change after months or years of conventional therapy, but in whom the blood picture was satisfactory) were given weekly doses of 1,000 μg. of vitamin B_{12}. Of these, 2 patients showed slight improvement, 4 showed no

improvement after 6 to 10 months' treatment, while one refused to continue with the injections.

In 2 cases the spinal-fluid level of vitamin B_{12} was determined by microbiological assay using *Lactobacillus leichmannii*. After a single injection of 1,000 μg. the level in the spinal fluid rose from 0·08 μg. per ml. to 0·25 μg. per ml. in 24 hours, while daily injections of 1,000 μg. of the vitamin produced a rise from 0·033 μg. per ml. to 2·7 μg. per ml. after 7 days. Urinary excretion of vitamin B_{12} was determined chemically following a single injection of 1,000 μg. in 4 patients with pernicious anaemia in relapse and in one patient with acute leukaemia. During the first 48 hours 51% to 98% of the dose was excreted.

From these results the authors conclude that in the treatment of pernicious anaemia single massive injections of vitamin B_{12} cannot be substituted for more frequent regular injection of smaller doses, and also that massive doses of the vitamin produce no greater improvement in subacute combined degeneration than do smaller doses, probably because of the rapid excretion observed in the urine when amounts above 25 to 50 μg. were given.

D. G. Adamson

454. **Oral Folic Acid Tolerance Test in Normal Human Subjects and Patients with Pernicious Anemia**

S. L. CLARK. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **82**, 25–28, Jan., 1953. 1 fig., 8 refs.

In order to investigate the possibility of deficient intestinal absorption of folic acid in pernicious anaemia, a folic acid tolerance test was carried out at Vanderbilt University School of Medicine, Nashville, Tennessee, on 17 healthy control subjects and 10 patients with pernicious anaemia. The test consisted in giving a dose of 0·5 to 2·0 mg. of folic acid in aqueous suspension 2 hours after breakfast, the concentration of folic acid in the blood serum being assayed microbiologically with *Streptococcus faecalis* before, and at intervals after, giving the test dose. The 1-mg. dose was sufficient to cause a rise in serum folic acid level in most of the normal subjects, though there was much variation in the individual responses—the peak serum level occurred at intervals ranging from 1 to more than 6 hours after the test dose, and the maximum level varied from 2 to 36 millimicrogrammes per ml. In the 10 cases of pernicious anaemia the results were similar to those in the controls, there being thus no evidence of a defect of gastro-intestinal absorption of folic acid in these patients.

M. C. G. Israëls

455. **Atypical Congenital Haemolytic Anaemia**

J. V. DACIE, P. L. MOLLISON, N. RICHARDSON, J. G. SELWYN, and L. SHAPIRO. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **22**, 79–98, Jan., 1953. 10 figs., 41 refs.

Writing from the Postgraduate Medical School of London, the authors describe in detail certain of the haematological and clinical findings in 12 patients with atypical congenital haemolytic anaemia. (The physical studies of the character of the haemoglobins, which are now so important in any analysis of haemolytic processes, will be reported separately.) The authors conclude that in all these patients the disease was genetically determined, although a familial incidence could be demonstrated in only 6 of the 10 families discussed. The cases were classified as follows: (1) non-spherocytic congenital haemolytic anaemia, 5 cases; (2) variants of hereditary spherocytosis, 4 cases; (3) a type with macrocytosis and leg ulcers, 1 case; (4) a variant of familial elliptocytosis, 1 case; (5) a type with "triangular" erythrocytes, 1 case. Splenectomy did not benefit the patients belonging to Groups 1, 3, and 5, but one of the patients in Group 2 and the patient in Group 4 were much improved by the operation

It is suggested that the disorder is due to inherent defects of the erythrocytes which result in a diminished life-span *in vivo*. In some of the present cases there was *in vitro* an accelerated rate of spontaneous haemolysis and an abnormal alteration in osmotic fragility on incubation at 37° C. The erythrocytes in this condition present distinctive morphological abnormalities and these are illustrated in photomicrographs. The literature is reviewed, and discussed in relation to the authors' cases.

Janet Vaughan

456. **Studies on Abnormal Hemoglobins. Electrophoretic Demonstration of Type S (Sickle Cell) Phenomenon**

K. SINGER and B. FISHER. *Blood* [*Blood*] **8**, 270–275, March, 1953. 2 figs., 18 refs.

457. **The Arterial Blood Gases, the Oxygen Dissociation Curve, and the Acid–Base Balance in Polycythemia Vera**

D. E. CASSELS and M. MORSE. *Journal of Clinical Investigation* [*J. clin. Invest.*] **32**, 52–59, Jan., 1953. 1 fig., 23 refs.

Studies of the blood in 17 patients with polycythaemia vera were made at the University of Chicago Clinics, and the results compared with those in normal subjects and in patients with polycythaemia secondary to congenital heart disease. Arterial oxygen saturation was normal in some patients with polycythaemia vera, thus showing that polycythaemia itself is not the cause of the arterial unsaturation. The oxygen dissociation of the blood was found to be normal in polycythaemia vera, and this was in contrast to a shift of the dissociation curve to the right in polycythaemia secondary to congenital heart disease. The acid–base equilibrium of the blood in polycythaemia vera usually differed little from the normal except for a decrease in the carbon dioxide content and in the combining power of the blood due to the higher concentration of erythrocytes in polycythaemia.

A. I. Suchett-Kaye

458. **The Significance of Hematogones in Blood, Bone Marrow and Lymph Node Aspiration in Giant Follicular Lymphoblastoma.** [In English]

N. ROSENTHAL, O. H. DRESKIN, I. L. VURAL, and F. G. ZAK. *Acta haematologica* [*Acta haemat. (Basel)*] **8**, 368–377, Dec., 1952. 8 figs., 51 refs.

From the Mount Sinai Hospital, New York, the authors report the haematological findings in 59 cases of follicular lymphoblastoma confirmed by lymph-node

biopsy or necropsy. In 10 of the cases unusual cells resembling small lymphocytes, but with a fine transverse cleft across the nucleus, were observed in the peripheral blood and bone marrow. Similar cells were identified in smears of lymph-node aspirate examined in 4 of the 10 cases. These cells, which have been designated amitotic lymphocytes or haematogones, have been observed in cases of follicular lymphoblastoma with increasing frequency in the last decade; they were not present in cases of lymphatic leukaemia or lymphosarcoma, and it is suggested that their presence is diagnostic of follicular lymphoblastoma and their identification of particular value in diagnosis when lymphoblastoma is associated with a lymphocytic blood picture. Haematogones were observed to be very highly radio-sensitive. The importance of using the smear technique is emphasized as these cells cannot be distinguished histologically in cut sections.

Mary D. Smith

459. **Triethylene Melamine in Human Malignant Disease. Results with Oral Administration of Enteric-coated Tablets**

E. PATERSON, P. B. KUNKLER, and A. L. WALPOLE. *British Medical Journal* [*Brit. med. J.*] **1**, 59–64, Jan. 10, 1953. 2 figs., 6 refs.

The authors report the results of administration of the cytotoxic substance triethylene melamine in enteric-coated tablets to patients suffering from Hodgkin's disease, chronic myeloid leukaemia, lymphatic leukaemia, and other diseases of the reticulo-endothelial system. Some beneficial effects were noted with doses of 0·2 to 0·3 mg. per kg. body weight. The authors wisely point out that this treatment should not be given to patients with leucopenia because of the great risk of damage to the haematopoietic system. Patients with lymphatic leukaemia were thought to respond better than did those with myeloid leukaemia. Renal function and hepatic function were investigated in some cases, and post-mortem examinations were carried out.

The authors found that the haematopoietic system was extremely sensitive to triethylene melamine, which affected particularly the lymphocytes, granulocytes, and platelets and very readily caused severe leucopenia, which they noted in 15 out of 22 cases of Hodgkin's disease. Of the 7 patients with chronic myeloid leukaemia, 5 died in 1 to 7 months, 2 being well for 5 and 6 months respectively. Remissions lasting 3 to 8 months were obtained in the 7 patients with lymphatic leukaemia, 3 of the 7 remaining well at the time of reporting.

John F. Wilkinson

460. **Myleran in Chronic Myeloid Leukaemia: Chemical Constitution and Biological Action**

A. HADDOW and G. M. TIMMIS. *Lancet* [*Lancet*] **1**, 207–208, Jan. 31, 1953. 4 refs.

" Myleran " (1:4-dimethanesulphonyloxybutane) is one of a series of compounds synthesized at the Chester Beatty Research Institute, Royal Cancer Hospital, London, on the assumption that their biological action might resemble that of the nitrogen mustards because of a common ability to alkylate. It has now been shown to be potent both in reducing the growth of the Walker carcinoma of rats and in limiting the myeloid activity of the bone marrow in rats and human subjects. Moreover, it has been shown that, unlike *x* rays and nitrogen mustards, myleran does not appreciably depress lymphocyte formation when given in doses sufficient to cause a reduction of 50% or more in the number of circulating neutrophil granulocytes. It would thus appear to be particularly suitable for the treatment of chronic myeloid leukaemia.

H. Payling Wright

461. **Myleran in Chronic Myeloid Leukaemia. Results of Treatment**

D. A. G. GALTON. *Lancet* [*Lancet*] **1**, 208–213, Jan. 31, 1953. 4 refs.

During a 2-year trial period, " myleran " [see Abstract 460] was administered orally to 19 patients with chronic myeloid leukaemia at the Royal Cancer Hospital, London. Two dosage schedules were used: (1) small daily doses (4 to 10 mg.) for a period of 4 to 16 weeks; and (2) a high daily dosage (100 to 150 mg.) given in one or more short courses lasting 1 to 6 days; in addition, 7 patients received maintenance therapy of 4 to 6 mg. daily for 1 to 12 months. A modification of the first schedule is now favoured, 4 mg. being given daily as long as haematological improvement continues. Weekly examinations were made in all cases, and the findings are clearly set out, both as case histories and in tabular form.

The author is guarded in his assessment of results, pointing out that radiotherapy has long been recognized as the best available palliative treatment for chronic myeloid leukaemia, and that any new remedy which is to compete successfully with it must be as efficacious, safe, easy to administer, and free from side-effects as this well-tried method. Myleran, however, appears to fulfil these criteria, the response in 3 previously untreated cases being comparable with the best results obtainable with radiotherapy. Symptoms dependent on anaemia and splenic enlargement were relieved in 10 patients, though in 7 others a favourable initial response was not maintained. Relief often occurred abruptly and was accompanied by a fall in leucocyte count. In previously irradiated cases the response was as great or greater than with radiotherapy. Granulocytopenia occurred in all instances, though the lymphocyte count was little affected. A satisfactory increase in haemoglobin level occurred, especially when a prolonged remission was induced, and bone-marrow activity returned towards normal. The improvement continued for 6 months or more in 9 cases. Myleran administration was always followed by some degree of thrombocytopenia, which in 2 instances produced a haemorrhagic state requiring blood transfusion In 3 cases, a second course was ineffective, which suggests that resistance to the drug may develop. Only in 3 cases did the response compare unfavourably with what might have been expected with radiotherapy.

[This series of 19 cases of leukaemia of very varied degrees of severity is insufficient for a satisfactory assessment of myleran treatment, but the results presented are highly encouraging.] *H. Payling Wright*

Respiratory System

462. Transient Undiagnosed Intrathoracic Lymphadenopathy in Apparently Healthy Persons

A. D. CHAVES and H. ABELES. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **67**, 45–58, Jan., 1953. 8 figs., 7 refs.

Amongst the many asymptomatic young adults examined at the tuberculosis clinics of the New York City Department of Health, in 20 cases routine chest radiography revealed intrathoracic lymphadenopathy which underwent spontaneous regression. In 10 of these patients there was no reaction to the intracutaneous injection of 1 mg. of old tuberculin. All remained in good health with no recurrence or visceral involvement for a mean period of 5 years. There was insufficient evidence to establish the aetiology in these cases, a benign transient hilar lymphadenopathy being apparently not uncommon. *D. Geraint James*

463. Myosarcoma of Trachea Associated with Riedel Struma

G. E. MCKENZIE and P. R. REZEK. *Archives of Otolaryngology* [*Arch. Otolaryng. (Chicago)*] **57**, 22–39, Jan., 1953. 10 figs., 22 refs.

While all primary tumours of the trachea are rare, sarcoma is among the rarest; Schiffner, reviewing the literature up to 1945, accepted only 36 cases as histologically proven. In this paper the authors report from the Jackson Memorial Hospital, Miami, a case of myosarcoma of the trachea, the rarest form of sarcoma in this region, which was associated with Riedel's struma, forming a combination never previously reported.

A stout, thick-necked woman of 54 years was admitted to the hospital with extreme dyspnoea. At bronchoscopy a large, dark, smooth, soft mass attached to the anterior wall of the trachea 20 cm. below the teeth was found blocking the airway. After a piece of the growth had been removed for section, tracheotomy was performed. Section showed a fast-growing, malignant, mesenchymatous tumour, and a provisional diagnosis of malignant mesenchymoma (angioplastic myosarcoma) was made. The patient was treated with deep *x*-ray therapy, and the tumour rapidly regressed; after 4 weeks no tumour was visible on bronchoscopy and the airway was adequate, but the tube was left *in situ* for 2 more weeks in case the growth recurred. Some 6 weeks later there was a return of the dyspnoea, and on bronchoscopy a tumour mass attached to the anterior wall and almost filling the lumen of the trachea was found higher up than the original mass. The tracheotomy was reopened and the patient seemed to make a fairly good recovery, but died of pneumonitis a fortnight later.

At necropsy it was found that the tumour mass had entered the trachea between the rings of cartilage, arising apparently from the bundles of unstriped muscle which connect the rings. This would account for the unusual nature of the growth. The presence of Riedel's struma was only detected post mortem, the diagnosis being made on the histological appearances, which showed a chronic inflammatory condition of the thyroid gland which had advanced to fibrosis and cystic degeneration, with almost complete disappearance of the thyroid epithelium, and contained giant cells of an unusual type. It is suggested that the condition is the result of chronic perithyroiditis, and some support is given to the view in this case by the presence of a well-marked inflammatory reaction in the attachments of the gland. *F. W. Watkyn-Thomas*

464. The Use of Penicillin and Sulfadiazine as Prophylactic Agents against Streptococcal and Non-specific Respiratory Infections among Recruits at a Naval Training Center

H. M. GEZON, J. S. COOK, R. L. MAGOFFIN, and C. H. MILLER. *American Journal of Hygiene* [*Amer. J. Hyg.*] **57**, 71–100, Jan., 1953. 10 figs., 28 refs.

An increase in the incidence of acute respiratory disease occurred early in January, 1952, among recruits in a U.S. Naval Training Centre, reaching a peak of 160·9 new cases per 1,000 per week in the first week of February, the majority of patients presenting a similar clinical picture with fever of sudden onset, cough, and minimal upper respiratory signs. In a survey made at this time, about 14% of a sample of 1,497 healthy recruits and 19% of 294 recruits reporting sick were found to have Group-A β-haemolytic streptococci in their nose or throat or both, while the rate in acutely ill patients was about 30%. (Atypical B or A-prime influenza virus was also isolated from some of these last cases.) Chemoprophylaxis was therefore started, about 5,000 recruits in one regiment receiving 125,000 units of buffered penicillin by mouth daily for 4 weeks, while 2 other regiments, totalling about 11,000 men, were divided into three roughly equal groups, the first of which (control group) received 0·3 g. of aspirin daily for 2 weeks, the second 1 g. of sulphadiazine daily for 2 weeks, and the third 125,000 units of penicillin by mouth daily for 4 weeks.

During the period of drug administration the incidence of Group-A streptococci in the nose and throat of healthy recruits taking penicillin fell to between one-third and one-half of that in the control group, whereas sulphadiazine had only a slight effect. Two weeks after the discontinuance of the drugs the incidence was virtually the same in all groups. At all stages of the outbreak Type-12 streptococci predominated, followed by Types 6, 3, 19, and 11. There was a sharp fall in the incidence of respiratory disease, starting immediately after prophylaxis began, which was partly attributable to a coincidental change of policy leading to the more frequent admission to hospital of men reporting sick, but also partly to the drug prophylaxis, since the incidence in the group given sulphadiazine was about

two-thirds, and in the group given penicillin about four-fifths, of that in the control group, sulphadiazine being more effective than penicillin in non-streptococcal infections. Moreover, Group-A steptococcal infection now accounted for only 15% of cases, most of which were diagnosed as common cold.

The frequency of reactions due to aspirin was 1 in 2,000, to sulphadiazine 1 in 450, and to penicillin 1 in 300; none was severe. There was no reduction in the incidence of sequelae of streptococcal infection with either drug. All of the 2,266 strains of streptococcus tested were sensitive to penicillin, and all but 3 (all Type-14) of 1,618 strains were sensitive to sulphadiazine.

M. Lubran

LUNGS AND BRONCHI

465. The Prevention of Postoperative Pulmonary Atelectasis

K. N. V. PALMER and B. A. SELLICK. *Lancet* [*Lancet*] **1**, 164–168, Jan. 24, 1953. 34 refs.

A method for the prevention of postoperative atelectasis which has been developed at the Middlesex Hospital, London, is described. The authors point out that postoperative atelectasis is due to a deficient expulsive mechanism, a reduction in bronchial calibre, or increase in secretion, and is more likely in the presence of one or more of the following: (1) a history of bronchitis; (2) clinical or radiological evidence of bronchitis; (3) infection of the upper respiratory tract in the 14 days preceding operation; (4) an abdominal operation.

The method consists in systematic bronchial drainage after the patient has inhaled, as a mist, 1 ml. of a 1% solution of isoprenaline. The foot of the patient's bed is raised at least 18 inches (46 cm.), and clapping and vibratory percussion are administered to the chest wall, especially the bases, the treatment being given for 5 or 10 minutes with the patient in each of the right and left lateral and prone positions. This treatment is repeated three times a day until no sputum is produced; it may have to be continued for up to 14 days before operation. In emergency surgery, where tipping is contraindicated, the isoprenaline only is given. After operation, when consciousness returns, inhalations are given 6-hourly and physiotherapy is started again as soon as the condition of the patient permits (usually after 6 to 12 hours). Treatment must be very thorough for 24 hours after operation and must be continued for at least 5 days. When there is evidence of atelectasis, treatment must be given hourly, and if re-expansion is not achieved within 12 hours, bronchoscopy must be considered.

The results obtained in a group of 90 patients treated by this method are compared with those obtained in a similar group of 90 patients who received breathing exercises before and after operation. Of the former group, 8 showed radiological evidence of atelectasis, compared with 39 in the latter group. The authors point out that these results can be obtained only when treatment is directed to the relief of the three aetiological factors simultaneously. *E. K. Brownrigg*

466. Segmental Aspiration Pneumonia and Bronchiectasis

K. D. F. MORLE and P. W. ROBERTSON. *British Medical Journal* [*Brit. med. J.*] **1**, 130–133, Jan. 17, 1953. 9 figs., 13 refs.

In a previous paper (*Brit. med. J.*, 1951, **2**, 994; *Abstracts of World Medicine*, 1952, **11**, 168) the authors called attention to the occurrence, in the course of upper respiratory infection, of segmental pulmonary collapse, often wrongly diagnosed as "virus pneumonia" or "atypical pneumonia". They now present further evidence to show that such an area of segmental collapse is often the forerunner of bronchiectasis. Owing to the unreliability of the previous history as elicited from the patient they were unable to determine exactly how often bronchiectasis was present before the respiratory infection occurred, but they have come to regard the infective episode as a precursor rather than a complication of bronchiectasis. In some cases they have observed repeated episodes of infection and collapse occurring in one segment, suggesting the possible course of the development of bronchiectasis.

Their experience leads them to believe, and the bronchograms reproduced illustrate their point, that bronchial dilatation, bronchial crowding, or bronchial plugging, present in the early stages of segmental aspiration pneumonia, may clear up with correct treatment, the bronchogram becoming normal. In the treatment of these cases the authors recommend accurate postural drainage, steam inhalations, and diathermy. The bronchial abnormalities, however, are not always reversible. *J. Naish*

467. Bronchiectasis: a Comparative Study

J. GORDON and P. C. PRATT. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **67**, 29–44, Jan., 1953. 36 figs., 10 refs.

Radiographs of excised specimens of bronchiectatic lung after the injection of contrast medium to outline the pulmonary arteries revealed differences between non-tuberculous and tuberculous bronchiectasis in the pattern of the pulmonary arterial tree. Whereas the fibrosis of chronic pulmonary tuberculosis caused marked obliteration of the vascular pattern, in non-tuberculous bronchiectasis the pattern was normal.

Bronchograms in cases of non-tuberculous saccular bronchiectasis showed that the bronchial dilatation extended to the periphery of the lung, whereas in tuberculous bronchiectasis it was limited to the medial two-thirds. The size of the bronchial lumen was found to change with inspiration and expiration in tuberculosis, but not in non-tuberculous cases. *D. Geraint James*

468. Precipitation by Pulmonary Infection of Acute Anoxia, Cardiac Failure and Respiratory Acidosis in Chronic Pulmonary Disease. Pathogenesis and Treatment

D. J. STONE, A. SCHWARTZ, W. NEWMAN, J. A. FELTMAN, and F. J. LOVELOCK. *American Journal of Medicine* [*Amer. J. Med.*] **14**, 14–22, Jan., 1953. 15 refs.

Otorhinolaryngology

469. **Rhinoscleroma**
W. B. HOOVER and G. D. KING. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **57**, 79–82, Jan., 1953. 1 fig.

As rhinoscleroma is rare in North America the present case is reported from the Lahey Clinic, Boston. A woman of 42, Russian-born but resident in the United States since the age of 5, was first seen in 1938 when she complained of three years' hoarseness and nasal crusting. A diagnosis of laryngeal carcinoma was suggested, but after laryngeal biopsy the pathologist's report was hyperkeratosis. (It is interesting to note that re-examination of the section in 1952 did not show any evidence of rhinoscleroma.) In 1944 she was seen again for a different complaint and was then still hoarse, and with left-sided nasal obstruction. After this she was not seen until 1950, when the nasal mass filled the left nostril, but she refused operation. A year later, however, she returned and the mass was removed. Section showed rhinoscleroma, and cultures yielded the Gram-negative von Frisch bacillus, which was found to be sensitive to terramycin and streptomycin, but not to aureomycin or to penicillin. The nasal condition cleared up entirely with local and systemic administration of streptomycin, suggesting that the von Frisch bacillus, and not a secondary invader, is the causal agent. Up to date 120 cases have been reported in the United States and Canada, but only 24 of the patients were native-born.

F. W. Watkyn-Thomas

470. **Effect of Cortical Lesions and Elimination of Retinal Impulses on Labyrinthine Nystagmus**
H. T. WYCIS and E. A. SPIEGEL. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **57**, 1–11, Jan., 1953. 6 figs., 5 refs.

It has been known for many years that removal of one cerebral hemisphere in rabbits facilitates nystagmus in the direction towards the side of injury, and diminishes it to the normal side. This " directional preponderance " applies to nystagmus produced by rotation or in response to calorization of the labyrinth. It had previously been shown that preponderance to the side of the lesion occurred in temporal-lobe tumours and also following section of the optic tract or electrolytic destruction of the external geniculate ganglion.

In this paper from the Temple University School of Medicine, Philadelphia, the authors attempt to answer two questions: (1) are any circumscribed regions of the cortex responsible for the production of directional preponderance? and if so, (2) do afferent retinal impulses moderate or increase the effects of cortical impulses on the vestibulo-ocular reflex arc? Directional preponderance may be the result of (*a*) increase of nystagmus to one side, (*b*) decrease to the opposite side, or (*c*) a combination of these factors, producing five varieties of nystagmus. The authors consider that the results noted by Fitzgerald and Hallpike (*Brain*, 1942, **65**, 115) in cases of tumour of the temporal lobe may have been due to damage to the optic radiation rather than to some definite lobar localization. In a series of experiments, including occipital and frontal lobectomy, on cats and dogs the present authors found that superficial lesions of the temporal or parietal lobes have slight, if any, effect on post-rotatory nystagmus, while deep lesions of the temporal lobe produce definite preponderance, apparently due to injury of pathways connecting the area striata with the brain-stem. After division of both optic nerves in 4 dogs there was increase of post-rotatory nystagmus to " a multiple of preoperative values ". Unilateral occipital lobectomy failed to produce definite directional preponderance when the retinal impulses were eliminated, but extensive frontal lobectomy could still produce directional preponderance to the side of operation. Lastly, it was found that unilateral decortication of one hemisphere caused much longer-lasting directional preponderance than did circumscribed lobectomy. This difference, in the authors' words, " suggests the participation of subcortical factors, besides the summated effect of the release of the vestibulo-ocular reflex arc from the influence of frontal and occipital cortical centers ". *F. W. Watkyn-Thomas*

471. **The Treatment of Deafness by Prosthesis**
H. G. KOBRAK. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol.* (*St. Louis*)] **61**, 1053–1066, Dec., 1952. 4 figs., 24 refs.

The author claims that it is possible, when the drum and middle ear have been damaged by infection, to improve the hearing by mechanical means. A disk of latex rubber may be used to cover a central perforation of the drum and will sometimes produce an improvement of 30 decibels for one or more of the speech frequencies of 256, 512, 1,024, and 2,048 c.p.s. A cotton-wool pellet soaked in oil is useful when there has been extensive destruction, as in a radical mastoid cavity, the pellet being moved about in the cavity until the best hearing is obtained; the cause of the improvement in this case is not properly understood. As the wool must be kept moist, the author recommends that it be soaked in " aquaphor " ointment, which contains a water-binding ingredient in the form of a group of cholesterol esters. Care must, of course, be taken that all appliances and instruments are sterile when they are introduced into the ear. *William McKenzie*

472. **Cancer of the Middle Ear**
V. M. DALLEY. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol.*] **4**, 193–196, Jan., 1953. 3 figs., 1 ref.

The treatment of a series of 26 cases of neoplasm of the mastoid, middle ear, or external auditory canal at the Royal Cancer Hospital, London, since 1936 is reviewed, 17 being cases of squamous-cell carcinoma and the

remainder a miscellaneous group including 2 cases of tumour of the glomus jugulare. In most cases surgical ablation of the accessible portion of the tumour preceded radiotherapy. The author describes the irradiation technique which has been evolved, teleradium therapy with a 10-g. unit being given from two ports on the affected side and 400-kV *x* rays from a single port on the opposite side. In this way a tumour dose of 6,000 to 7,000 r is built up in about 6 weeks. The results in cases of squamous-cell carcinoma confirm the view that the prognosis is bad, most patients dying of recurrent local disease with consequent cachexia rather than from widespread dissemination of the disease. In the miscellaneous group, however, the prognosis is decidedly better, all but one patient being alive without recurrence, though in no case has the follow-up period exceeded 5 years in this group. *E. Stanley Lee*

473. **Chronic Suppurative Otitis Media and the Antibiotics.** (Le otiti medie purulente croniche e gli antibiotici)

P. SALOMONE. *Valsalva. Rivista bimestrale di oto-rino-laringoiatria* [*Valsalva*] **28**, 320–341, Dec., 1952. 29 refs.

The author has carefully followed up 400 cases of chronic otitis media which had been treated at the Morvillo Hospital, Naples, and in private practice by all available methods, including intensive local and parenteral administration of antibiotics. He found that, with or without antibiotics, 80% had been cured but that the remaining 20% still required surgical treatment, and included cases complicated by cholesteatoma and polyp; in this group the cure-rate was 70%. In addition to other known causes responsible for the development of chronicity he emphasizes the irrational use of antibiotics during the acute stage.

The author suggests the following nomenclature: protympanitis for cases of inflammation with anterior inferior perforation, mesotympanitis for those with central perforation, and epitympanitis for those with marginal perforation. The last-named cases, especially if combined with cholesteatoma or with symptoms of other complications, are usually resistant to antibiotics and require operation. Factors influencing the decision to operate are: the morbid-anatomical condition of the temporal bone, the findings on radiological examination and clinical observation, bacteriological findings (including any sensitivity to antibiotics), and the condition of the inner ear as ascertained by modern methods of audiometry. *C. Eisinger*

474. **Sarcoma of Larynx. Report of Two Cases**

K. L. DIEHL. *Archives of Otolaryngology* [*Arch. Otolaryng. (Chicago)*] **57**, 40–43, Jan., 1953. 11 refs.

Sarcoma of the larynx is a rare condition. Clerf in 1946 maintained that the ratio of laryngeal sarcoma to laryngeal carcinoma is not more than 1 to 100. In the present paper from Rochester, New York, the author stresses the fact that in both the cases reported the appearance on endoscopy was that of a benign growth. In the first case, seen in March, 1951, a fibroma was diagnosed on biopsy, and it was only on account of the size of the mass, which made it difficult to remove endoscopically, that thyrotomy was done. Section of the mass showed a localized fibrosarcoma within it. Recurrence took place 3 months later, and complete laryngectomy was then performed. In the second case (March, 1952) the biopsy specimen removed endoscopically was diagnosed as fibrous tissue, and a second specimen was regarded as showing chronic inflammation rather than a malignant growth. In view of the finding in the first case, however, as much as possible of the mass was removed under suspension laryngoscopy, and was recognized as sarcoma. Total laryngectomy was performed and a permanent tracheal opening made. Both patients were well at the time of this report.

The author emphasizes that, histologically as well as clinically, sarcoma may be mistaken for a benign tumour because, as Clerf pointed out, sarcomatous tumours often have a peripheral area of benign tissue. In the author's view thyrotomy and excision of the sarcoma alone are inadequate treatment and total laryngectomy should be performed. *F. W. Watkyn-Thomas*

475. **Intramucosal Epithelioma of the Larynx**

A. P. STOUT. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **69**, 1–13, Jan., 1953. 10 figs., 16 refs.

After referring to Bowen's pioneer work on intraepidermal cancer, the author reports that, of 312 cases of laryngeal epithelioma examined histologically at the Presbyterian Hospital, New York, between January, 1940, and June, 1950, 57 were of the intramucosal type. In 9 instances the lesion occurred in a recurrent papilloma, in 19 there was also invasive growth, and in the remaining 29 cases the growth was limited to the surface mucosa or was extending only into its glands. According to the author intramucosal cancer can affect any part of the larynx, intrinsic or extrinsic, but is most commonly found on the cords. He describes its histological and clinical characteristics, and states that multiple biopsies are usually required for a satisfactory diagnosis.

From the results of treatment in the present series [for details of which the original paper should be consulted] the author concludes that although local excision or laryngofissure with removal of a single cord often proves successful, the selection of cases for such treatment is very difficult, and laryngectomy is almost inevitable if it fails. Theoretically, the best form of treatment " is one which will remove or destroy all of the mucous membrane together with the mucous glands and their ducts ". This may be achieved by total laryngectomy, which " will probably cure every case of intraepithelial epithelioma ", but only at the cost of severe mutilation, and in the author's opinion the necessary destruction of mucosa can be obtained more effectively by means of radiotherapy. This form of treatment was not given a fair trial in the present series, being reserved for cases regarded as unsuitable for surgery, but although 5 out of the 10 patients with non-invasive tumours so treated died within 5 years, in 4 of these cases death was due to heart disease and in the fifth to perichondritis resulting from improper dosage, the remaining 5 patients being alive and well.

H. D. Brown Kelly

Urogenital System

476. **Observations on Effect of Methantheline (Banthine) Bromide in Urological Disturbances**
J. LAPIDES and A. I. DODSON. *Archives of Surgery* [*Arch. Surg.* (*Chicago*)] **66**, 1–9, Jan., 1953. 7 figs., 4 refs.

In the normal person, after the age of infancy, as the bladder fills with urine stretch receptors in the bladder wall initiate impulses which travel to the spinal cord along the sensory fibres of the pelvic nerves. In the spinal cord these sensory impulses impinge upon the motor neurones of the bladder (located at S2, S3, and S4); they are also conducted along the ascending sensory tracts to the higher centres of the brain. The lower reflex arc does not operate to cause contractions in the bladder in response to these stimuli, because the cortical regulating centre exercises a constant inhibiting effect. It is only when this inhibiting effect is removed by the voluntary desire to micturate that the lower motor neurones do respond to these sensory afferent impulses and the act of micturition is initiated. In neurogenic enuresis there is a lesion of the cortical regulating centre, so that the lower motor neurones are not effectively inhibited. The sensory impulses impinging upon these motor neurones activate some of them to cause contraction of the bladder. If the number of motor neurones so activated is few, the degree of contraction will be minimal and will not produce voiding, although the patient may be conscious of the contraction.

Methantheline bromide blocks motor impulses at the ganglion and also at the post-ganglionic cholinergic nerve endings, which in the case of the bladder pass along the parasympathetic fibres of the pelvic nerves. A dose of 150 to 200 mg. of methantheline bromide given intravenously to a normal person produces complete bladder paralysis with acute retention for 3 to 5 hours. When given to a patient with neurogenic enuresis it abolishes all the minimal contractions which are short of voiding contractions, and it also prolongs the time before a voiding contraction occurs, so that there is an increase in apparent bladder capacity. The patient is able to void at will, with no residual urine; in this way the frequency of micturition can be decreased to within normal limits and there is no incontinence. These results have been observed in a series of 30 cases of " uninhibited neurogenic enuresis " seen at the University of Michigan Medical School, Ann Arbor. It is important to differentiate between cases of neurogenic enuresis and those of psychogenic enuresis, for in the latter type of case methantheline bromide has no effect. Nor has it any effect in other types of incontinence or frequency, such as stress incontinence, overflow incontinence, or incontinence from injury to the internal or external sphincters.

In further studies methantheline bromide was found also to relieve the pain in certain cases of renal and ureteric colic and of some bladder conditions, although the mechanism of this relief is as yet not understood. In cases of interstitial cystitis such as those associated with Hunner's ulcer temporary, but no lasting, relief was given by the use of this drug. In some cases of small-capacity bladder, such as the spastic reflex neurogenic bladder of the paraplegic and spastic bladder after catheter decompression, methantheline bromide brought about an increase in the effective bladder capacity.

No harmful effects of the drug were observed in the patients under treatment, but certain precautions should be observed, particularly in cases of glaucoma and severe cardiac disease and in patients with an enlarged prostate, in whom acute retention may be precipitated.

James Kemble

477. **Excretion of Ammonium in Cases of Acute Tubular Necrosis with Acidosis and Alkaline Urine**
H. L. DE OLIVEIRA. *Metabolism* [*Metabolism*] **2**, 36–46, Jan., 1953. 8 figs., 11 refs.

Acidification of the urine through the carbonic anhydrase system has been shown to be a direct consequence of lowered bicarbonate concentration in the glomerular filtrate. Increased acidity of the tubular fluid might, on theoretical grounds, lead in turn to increased ammonia production, the process being one of diffusion of intracellular ammonia into the acid tubular fluid. Evidence against this view is provided by the study of the renal defect in acute tubular necrosis in which an alkaline urine is produced in the presence of acidosis.

The author has investigated 4 cases of acute tubular necrosis, one following blood transfusion and 3 due to mercuric poisoning, at the Hospital das Clínicas, São Paulo, Brazil. Observations were also made on 2 patients with normal kidney function. Urinary excretion of titratable acid and ammonium was determined before and during acidosis induced by the oral administration of ammonium chloride. An inability to acidify urine was manifest as early as the onset phase preceding anuria. Ammonium excretion was reduced at the beginning of the early diuretic phase in proportion to the low rate of urine production. With increasing urinary output the ammonium excretion increased to high normal values, though the urine remained alkaline.

K. O. Black

478. **Renal Endometriosis, a New Clinical Entity. Symptoms and Pathogenesis.** (L'endométriose rénale, nouvelle entité anatomo-clinique. Symptômes et pathogénie)
E. BLUM and L. FRUHLING. *Journal de Chirurgie* [*J. Chir.* (*Paris*)] **69**, 19–37, Jan., 1953. 16 figs., 34 refs.

From the University Surgical Clinic, Strasbourg, the authors present 2 personal cases of renal endometriosis in women aged 22 and 42 respectively, together with 2 further cases from the literature; in only one of these

cases was there associated pelvic endometriosis, which eventually necessitated subtotal hysterectomy and excision of cysts of the ovary. The first case presented with a painful swelling in the loin which was not related to the menses; nephrectomy revealed a cystic mass in the upper pole, full of old blood. The next 2 patients complained of pain in the loin which coincided with the menses. In both these cases pyelography revealed a small atrophic kidney with a dilated pelvis, and at nephrectomy a chronic ascending pyelonephritis was found. In one kidney there was a small nodule in the superior pole the size of a cherry in which histological examination showed typical endometrial tissue. The fourth case presented with painless profuse haematuria not related to menstruation, and ascending pyelography revealed a dilated upper calyx. At operation there was a cystic swelling in the superior pole which was aspirated and found to contain 20 ml. of chocolate-coloured fluid.

The authors discuss the different theories of the pathogenesis of endometriosis. Their own theory is a modification of the theory of metaplasia, in which they postulate first a dedifferentiation in anaplastic tubules, followed by the development of renal tubules, and eventually metaplasia to glandular endometrial tubules. This metaplasia, they believe, is mediated by two factors, one of which is endocrine and the other chronic inflammation. *K. Whittle Martin*

479. **On the Occurrence of Skeletal Disorders in Cases of Long Standing Renal Failure**
C. L. JOINER and M. G. THORNE. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **102**, 1–35, 1953. 22 figs., bibliography.

In this paper 4 cases of renal osteodystrophy seen at Guy's Hospital, London, are described in detail. In the 3 cases which came to necropsy the renal picture was that of pyelonephritis. Of the 3 women patients, 2 suffered from menorrhagia. In one case there were widespread metastatic calcifications in the arteries and subcutaneous tissues, around several joints (easily mistaken for gouty tophi), and in the conjunctivae and lymph nodes. It is suggested that the decreased alkali reserve which was a feature in this series, as in other cases reported, may be caused by the inability of the diseased kidneys to synthesize ammonia; to neutralize excess acid before excretion, calcium from the bones is mobilized. Sodium is mentioned as an alternate base; in 2 of the patients in this series the serum sodium level was noted to be below normal. It is also general experience that hypertension is unusual in patients suffering from renal osteodystrophy, whereas calcium or sodium depletion and hypertension are both found in the so-called " salt-losing nephritis ". It is suggested that, as the absence of hypertension in chronic renal failure may contribute to the longevity of the patient, calcium is eventually drawn upon from the skeleton, leading to the appearance of renal osteodystrophy. Other hypotheses to account for the bone lesions postulate a primary retention of phosphate, causing lowering of the serum calcium level and thus stimulating the parathyroid glands to mobilize calcium from the bones.

Of the 4 patients in the present series, 3 received large doses of calcium and alkali by mouth, as described by Albright (*Bull. Johns Hopk. Hosp.*, 1940, **66**, 7). Though this treatment failed to give any relief in 2 patients who had advanced disease, it apparently increased the alkali reserve, with temporary decrease in serum phosphate level, and led to symptomatic improvement in one case. *G. W. Csonka*

480. **Intravenous Urography in Tumours of the Neck of the Bladder.** (Die intravenöse Urographie bei der Blasenhalsgeschwulst)
E. FRIEDHOFF. *Archiv für klinische Chirurgie* [*Arch. klin. Chir.*] **274**, 132–138, Jan. 20, 1953. 2 figs., 21 refs.

Characteristic appearances are described in 100 cases of obstruction of the bladder neck investigated by intravenous urography at the University Surgical Clinic, Cologne. Typically, the distance between the bladder shadow and the symphysis is seen to be increased, while the contour of the bladder-neck outline is often clearly defined. Trabeculation is shown by irregularity of the marginal outline, and an important feature in obstruction may be a " fish hook " ending of the lower segments of the ureters, indicating elevation of the bladder by a prostatic tumour.

The author considers intravenous urography to have limited value in comparison with water and concentration tests as an index of renal function, but recommends that it should be carried out before deciding to operate in all cases of bladder-neck obstruction. *J. D. Fergusson*

481. **Total Adrenalectomy for Reactivated Carcinoma of the Prostate**
J. H. HARRISON, G. W. THORN, and D. JENKINS. *New England Journal of Medicine* [*New Engl. J. Med.*] **248**, 86–92, Jan. 15, 1953. 3 figs., 7 refs.

In this paper, from the Peter Bent Brigham Hospital and Harvard University, Boston, 7 cases in which bilateral adrenalectomy was carried out for carcinoma of the prostate are described. All the patients were suffering from a recurrence of carcinoma 6 months to 5 years after orchidectomy and oestrogen therapy. In one patient there was local and regional recurrence and in 6 there were osseous metastases with severe pain.

After total adrenalectomy marked clinical and objective improvement was observed in 6 of the patients; in the remaining patient, aged 50 years, the disease progressed unabated. One patient was alive and well 17 months after operation, although the biopsy material still revealed the presence of an adenocarcinoma of the prostate. It is pointed out that while the improvement was striking in these cases, it was relatively not so pronounced as that observed after primary orchidectomy and oestrogen therapy. The 17-ketosteroid excretion fell to an average of 4 to 6 mg. in 24 hours. The authors give details of the doses of cortisone administered before, during, and after operation. *Thomas Moore*

See also Pathology, Abstract 320.

Endocrinology

482. **The Rate of Growth in Progeria. With a Report of Two Cases**
J. V. COOKE. *Journal of Pediatrics* [*J. Pediat.*] **42**, 26–37, Jan., 1953. 9 figs., 23 refs.

After describing 2 cases of progeria which he has observed personally, the author gives details of height, weight, and age in 22 cases which have been reported between the years 1886 and 1952. Graphs drawn up from these data to show the rate of growth in height and weight in cases of progeria are then compared with normal growth curves compiled from the Harvard and Iowa data for Americans in the first two decades. After an almost normal increase during the first year, the weight of children with progeria becomes stabilized and thereafter remains about that of a normal child in the second year, the maximum recorded being the normal 3-year-old level. The height in cases of progeria increases slowly but regularly during the first decade, reaching eventually that of the normal child of 4 to 5 years, which appears to be the maximum attainable.

In fatal cases of progeria the most marked lesions have been found in the cardiovascular system, and especially in the coronary arteries. No constant change has been found in the pituitary gland so that, although it is recognized that dysfunction may occur without any demonstrable morphological change, the hypothesis that progeria is related to pituitary hypofunction must be regarded as purely speculative. It is suggested that the unknown factors which normally cause arrest of growth at maturity may in progeria be brought into play prematurely owing to some congenital defect.

Jas. M. Smellie

483. **A Syndrome of Testicular Insufficiency Characterized by the Complete Absence of Leydig Cells, Disturbance of Germinal Epithelium and Decreased Urinary Gonadotrophins.** [In English]
E. B. DEL CASTILLO, A. TRABUCCO, and A. ONATIVIA. *Acta endocrinologica* [*Acta endocr.* (*Kbh.*)] **12**, 8–22, Jan., 1953. 7 figs., 29 refs.

The authors report 5 cases of a rare type of testicular insufficiency which were observed at the Rivadavia and Alvear Hospitals in Buenos Aires. They presented the following syndrome: pronounced primary and secondary eunuchoidism, complete absence of the Leydig cells with other modifications of the germinal epithelium (Sertoli cells, however, remaining), and diminished excretion in the urine of the gonadotrophic hormones and of the 17-ketosteroids. Each case was investigated, a general clinical examination, microscopy of the spermatic fluid, testicular biopsy, and estimation of the urinary hormone excretion being carried out.

Apart from minor variations noted in one case, which are attributed by the authors to the administration of testosterone, the findings were materially similar.

Several alternative theories of the causation of this syndrome are discussed by the authors, who express themselves in favour of the suggestion, made by Albright, that there is a second testicular hormone, the " X " hormone, the origin of which has been attributed to the Sertoli cells, though this remains to be proved. This hormone is thought to have a trophic action on the germinal epitheluim, both directly and by stimulation of the anterior lobe of the pituitary gland, and the present authors suggest that the syndrome described may be due to a failure in production of the " X " hormone resulting from decreased secretion of pituitary follicle-stimulating hormone after puberty.

H. L. Attwater

THYROID GLAND

484. **Malignant Exophthalmos. Muscular Changes and Thyrotrophin Content in Serum.** [In English]
G. ASBOE-HANSEN, K. IVERSEN, and R. WICHMANN. *Acta endocrinologica* [*Acta endocr.* (*Kbh.*)] **11**, 376–399, Dec., 1952. 4 figs., 32 refs.

To throw some light on the pathology of malignant exophthalmos, the authors, working at the University Hospital and the State Serum Institute, Copenhagen, examined various skeletal muscles histochemically and determined the thyrotrophin concentration in the blood serum by biological assay in a series of cases including 11 patients with malignant exophthalmos, 21 with Graves's disease, 7 with myxoedema, and 25 subjects without pituitary or thyroid disorders. It was found that considerable amounts of acid mucopolysaccharide were present in the interstitial muscular connective tissue of patients with malignant exophthalmos and those with myxoedema, indicating a generalized muscular lesion. The serum level of thyrotrophin was significantly raised in 9 out of 10 patients with malignant exophthalmos as compared with 6 normal subjects. The authors suggest that these findings indicate a thyrotrophic origin for malignant exophthalmos.

E. Godtfredsen

485. **Diagnosis of Intrathoracic Goitre**
G. ANSELL. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol.*] **4**, 197–206, Jan., 1953. 6 figs., 10 refs.

An intrathoracic goitre presents the radiological picture of a superior mediastinal tumour which must be distinguished from an aortic or other aneurysm, enlarged mediastinal lymph nodes, a thymoma, an oesophageal diverticulum, a mediastinal abscess, a dermoid or other cyst, and from certain rare tumours such as those of the oesophagus. For this purpose the examination should always include a barium swallow, and certain characteristic features may be observed.

Intrathoracic goitre tends to depress the aortic knuckle, making a distinct angle with it which changes if the goitre

rises on deglutition. The trachea is usually displaced laterally or compressed from side to side. Areas of calcification, usually irregular, are present in about 25% of cases. Very rarely the tumour may extend down to the diaphragm, the appearences then resembling those of right-sided cardiac enlargement.

To assess the possible value of radioactive iodine (^{131}I) in diagnosis, 15 cases of suspected intrathoracic goitre were examined by the author at the University of Liverpool with a collimated Geiger counter 24 hours after a a tracer dose of ^{131}I had been given. (It is noted that the patient should not have been taking iodine recently and that there should not have been any recent radiological examination with iodized oil.) It was concluded that the demonstration of ^{131}I-concentrating tissue in the chest provides definite evidence of an intrathoracic goitre, but that negative findings do not exclude the diagnosis, since such tumours often undergo cystic or degenerative changes. *E. Stanley Lee*

486. **Relationship of Gonadal Imbalance to Thyroid Disease**

F. P. Ferrer and T. H. McGavack. *American Journal of Surgery* [*Amer. J. Surg.*] **85**, 67–70, Jan., 1953. 3 figs., 7 refs.

The incidence of gonadal dysfunction was studied in 467 patients with various thyroid disorders admitted to two hospitals in New York between 1945 and 1949. Of these patients, 84·2% were females and 15·8% males, 78·6% being married and 21·4% single; 65·3% were between 30 and 60 years of age, the highest incidence being between the ages of 40 and 50 (26·3%).

In 180 cases (38·5%) there was a history of mastitis or of tubal, ovarian, or uterine disease in the females, and of prostatism, undescended testicle, inguinal hernia, mastitis, castration, or absence of secondary sex characters in the males. In 104 of the women there was a history of menstrual irregularity (patients with postpartum menstrual irregularities and with dysmenorrhoea or sterility or menopausal symptoms were excluded from the analysis). In 88 of the women hysterectomy had been performed from 6 months to 26 years (average 5 years) before the onset of the thyroid disorder. The total incidence of previous gonadal disorders was thus 79·6%, compared with an incidence of 21·2% among a group of patients with osteoarthritis.

A history of previous gonadal disorder was obtained in 163 (87·6%) of 186 cases of non-toxic adenoma, 29 of 34 cases of simple adenoma (78·4%), 99 of 126 cases of toxic adenoma, 32 out of 41 cases of Graves's disease, 15 out of 34 cases of carcinoma of the thyroid, 23 out of 26 cases of myxoedema, 6 out of 13 cases of thyroglossal cyst, and 6 out of 7 cases of thyroiditis. [It is not clear what the distinction is between "non-toxic adenoma" and "simple adenoma"; presumably "Graves's disease" indicates primary thyrotoxicosis.]

The authors emphasize the functional relationship between the thyroid gland and the gonads. Thyroid disease, they say, is more liable to follow than to precede disturbances in the genital tract, and the basal metabolic rate fluctuates with various phases of the menstrual cycle. They cite experiments showing that administration of thyroid hormone improves gonadal function in partially or completely castrated animals, and that it may either increase gonadotrophic secretion or impair the response of the gonads to gonadotrophic hormone in animals. It is only at the extremes of thyroid hormone production, they say, that recognizable disturbances in the function of the gonads are seen.

[This paper is of limited value, in so far as it attempts to correlate a miscellaneous group of thyroid disorders with an even more miscellaneous group of gonadal disorders, many of which do not even entail endocrine dysfunction. No attempt is made, for instance, to correlate specific menstrual disturbances with specific disturbances of thyroid dysfunction. The article does, however, emphasize the need for further investigation of the relationship between thyroid and gonadal function, of which we are at present very ignorant.]

Robert de Mowbray

487. **Detection of Concealed Thyroid Disease by Tracer Technique**

L. Reynolds, K. E. Corrigan, and H. S. Hayden. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 368–371, Jan. 31., 1953, 7 figs., 5 refs.

DIABETES MELLITUS

488. **Potassium in the Treatment of Diabetic Coma**

J. H. Crampton, G. W. Mellinger, and L. J. Palmer. *Diabetes* [*Diabetes*] **2**, 1–6, Jan.–Feb., 1953. 3 figs., 15 refs.

While emphasis on the early and adequate administration of insulin and fluid therapy, coupled with the introduction of antibiotics, has greatly reduced the mortality from diabetic coma in recent years, the demonstration of profound disturbances of potassium metabolism suggests that it might be reduced still further by their correction. In diabetic acidosis potassium first moves out of the intracellular space as a result of increased glycogenolysis and gluconeogenesis and is washed out by the diuresis; but later, owing to terminal dehydration, there may be hyperpotassaemia in spite of total body depletion of potassium. During treatment on the other hand, rehydration, together with re-establishment of urinary excretion and return of potassium into the cells, results in a fall in the serum potassium level, and although this is not usually enough to cause trouble, signs of hypopotassaemia may occur in the form of skeletal muscular paralysis, sometimes with respiratory distress, vascular collapse, and intestinal ileus. Various opinions as to the best method of prevention and treatment of this condition are noted, the authors themselves giving potassium salts orally as a routine. Their plan of treatment in diabetic coma is to give an initial dose of insulin based on a clinical evaluation and to supplement this later so that the dosage in units in the first 2 hours is half the number of milligrammes of sugar per 100 ml. of blood in the first sample. (This is modified for the

young, the aged, and those thought to be insulin-sensitive.) Physiological saline is given intravenously at first, no glucose being given until an adequate fall in blood sugar level has been obtained. An indwelling catheter is always inserted into the bladder and output noted. After 4 hours, if the urinary output is adequate, 80 ml. of a 10% solution of dibasic potassium phosphate in 100 ml. of water is put into the stomach through a tube, and thereafter 10 to 20 ml. is given hourly as soon as the patient can take fluids without nausea. Potassium may have to be given intravenously (as a 1% solution of potassium chloride in water) if the patient is unable to take it by mouth

The results in 32 cases treated without potassium are compared with those in 53 treated with potassium, the serum carbon dioxide combining power being less than 10 mEq. per 100 ml. in all cases. In the former series there were 3 deaths and in the latter none, and although the authors admit that other factors may have contributed, they " feel that the free use of potassium salts has been a significant factor in the absence of mortality reported here ". They give 3 illustrative case histories.

R. St. J. Buxton

489. **Parallel Relation of Hyperglycemia and Hyperlipemia (Esterified Fatty Acids) in Diabetes**

E. F. Hirsch, B. P. Phibbs, and L. Carbonaro. *Archives of Internal Medicine* [*Arch. intern. Med.*] **91**, 106–117, Jan., 1953. 8 figs., 10 refs.

In 1950, two of the present authors (Hirsch and Carbonaro, *Arch. intern. Med.*, **86**, 519; *Abstracts of World Medicine*, 1951, **9**, 279), carried out fractional estimations of the serum lipids in animals subjected to pancreatectomy and found that in diabetic lipaemia the triglyceride fraction is increased most, while the cholesterol and phospholipid fractions are increased slightly or not at all. Studying the effects of a fatty meal in normal adults and in diabetic patients, these workers found a postprandial rise in the serum level of esterified fatty acids, but failed to observe any parallel rise in the serum cholesterol level. They therefore concluded that cholesterol analyses gave no indication of the postprandial lipaemia disclosed by the quantitative analysis of the serum level of esterified fatty acids.

The present authors, writing from the University of Chicago, point out that the need for careful regulation of the diet with insulin control of the diabetic is now disputed. Some workers hold that the blood sugar level should be strictly controlled by diet and insulin, while others hold that hyperglycaemia and glycosuria cannot be proved to be harmful. The dispute has concerned, particularly, the part played by hyperglycaemia in the development of atherosclerosis. All workers stress the significance of the blood lipid level in the evolution of this condition, and the high incidence of atherosclerosis in diabetic patients has long been recognized.

In order to determine whether under varying conditions the serum fatty acid content bore any constant relation to the blood sugar level, the authors estimated simultaneously the serum fatty acid and blood sugar levels under varying conditions of diabetic stabilization. For the fatty acid estimations they used the method of Bauer and Hirsch, and for the blood sugar estimations the method of Folin and Wu adapted for spectrophotometric analysis. The patients included 4 who were made hyperglycaemic by withholding insulin, 3 who were given fatty meals when hyperglycaemic and again when the blood sugar level was normal, one who was studied during a prolonged period of fluctuation of the blood sugar level, and 2 in whom the blood sugar content was unstable as a result of changes in diet and in the insulin dosage. A direct relationship was found between hyperglycaemia and hyperlipaemia in diabetic patients, the esterified fatty acid level rising and falling with the blood sugar level. Estimations of the blood cholesterol level showed no similar relationship.

The authors suggest that in the light of current views on the aetiology of atherosclerosis, their observations would indicate the importance of maintaining a normal blood sugar level in diabetic patients in order that the blood lipid content may be kept within the high-normal range and the development of degenerative vascular disease delayed.

J. Lister

490. **Insulin and the Permeability of Cell Membranes to Glucose**

E. J. Ross. *Nature* [*Nature (Lond.)*] **171**, 125, Jan. 17, 1953. 2 refs.

In this brief report from the Institute of Ophthalmology, London, evidence in support of the concept that insulin acts by increasing the permeability of cell membranes to biologically important sugars by accelerating an enzymic transport mechanism and so promotes the transfer of glucose through the cell wall is adduced from studies of the uptake of glucose by the isolated rabbit lens. The lenses were incubated for 3 hours in a suitable buffer solution to which had been added glucose to give a concentration equal to that in the aqueous humour. In the absence of insulin the uptake of glucose was 0·202 mg. per g. of lens substance per hour; in the presence of 1 unit of insulin it was 0·71 mg. per g. per hour, an increase of 250%. Glucose uptake by homogenates of lens tissue was 0·269 mg. per g. per hour. It is suggested that the hyperglycaemia of diabetes mellitus is the result of the inability of glucose to enter the cells rather than of a failure of intracellular enzymic oxidation.

F. W. Chattaway

491. **A New Long-acting Insulin. A Preliminary Trial of " Lente " Novo Insulin**

R. D. Lawrence and W. Oakley. *British Medical Journal* [*Brit. med. J.*] **1**, 242–244, Jan. 31, 1953. 5 figs., 1 ref.

It has been shown by Danish workers that insulin in the presence of 1 mg. of zinc per 1,000 units is less soluble at blood *p*H than protamine insulin, provided that anions such as phosphate and citrate are not present. With acetate instead of phosphate as buffer, three preparations of zinc insulin have been produced called " semi-lente," " lente," and " ultra-lente " insulin, and in the present paper the authors report a trial of lente insulin at King's College Hospital, London. The range

of activity of these insulin preparations appears to depend on the ratio of amorphous to crystalline insulin and upon the size of the crystals; the action of amorphous insulin is shorter than that of crystalline, while the larger size of the crystals, the greater the duration of activity. The semi-lente type has the shortest and the ultra-lente the longest duration of activity.

The clinical trial was carried out on 11 adults with severe diabetes whose ages ranged from 25 to 92 years and all of whom were reasonably stable on a total daily dose of insulin of 28 to 76 units; 6 of the patients were taking a mixture of soluble insulin and protamine zinc insulin, 2 were receiving two doses of soluble insulin, 2 a single dose of protamine zinc insulin, and one was receiving globin insulin. When control was established the blood sugar content was determined at four different times of day and the urine more frequently. The patients' treatment was then changed to a single dose of lente insulin, given before breakfast in the same total dose, and after at least 2 days the blood and urine tests were repeated at the same times. It was found that the fasting blood sugar level in all cases and the midday level in 9 of the 11 cases were as satisfactory with lente insulin as with the other preparations. No severe hypoglycaemia or other undesirable side-effect was observed.

The authors consider that their results justify the claim that lente insulin has a prolonged action and, at the same time, " exerts a short hypoglycaemic action, comparable with that of soluble insulin alone or mixed with protamine zinc insulin ". *J. Lister*

492. **Clinical Vitamin Deficiencies in Patients with Diabetes Mellitus**
B. BEIDLEMAN. *Journal of Clinical Nutrition* [*J. clin. Nutrit.*] **1**, 119–123, Jan., 1953. 9 refs.

ADRENAL GLANDS

493. **Inhibition of Rapid Production of Antibody by Cortisone. Study of Secondary Response**
E. E. FISCHEL, J. H. VAUGHAN, and C. PHOTOPOULOS. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **81**, 344–348, Nov., 1952. 1 fig., 26 refs.

In this paper from Columbia University and the Presbyterian Hospital, New York, the authors show that cortisone markedly inhibits the synthesis of antibody protein during elicitation of a specific anamnestic or secondary immune response. In the experiments described rabbits which had been immunized to purified egg albumen 2 months previously were given a stimulating dose of antigen in the form of an intravenous injection of alum-precipitated egg albumen containing 1 mg. of nitrogen. Their antibody levels were determined 12 and 6 days before the injection and on the 5th and 13th days after it. Cortisone was given intramuscularly to 8 of the animals in daily doses of 25 mg., starting 4 days before the injection of antigen, and 7 comparable animals not given cortisone acted as a control group.

It was found that 5 days after the antigen injection a sharp rise occurred in the antibody levels of the control animals, but those of the cortisone-treated animals remained about the same or were even slightly reduced by the 5th day. By the 13th day further increases had occurred in the control group, but there was still no change in the cortisone-treated group. Present knowledge of the effect of cortisone on antibody synthesis is briefly discussed, and it is considered that there is no reason to abandon the concept of Landsteiner that immunological reactions are chemically specific.

C. L. Cope

494. **The Effects of Cortisone and Adrenocorticotrophic Hormone on Experimental Inflammations in the Human Skin**
R. R. H. LOVELL, H. C. GOODMAN, B. HUDSON, P. ARMITAGE, and G. W. PICKERING. *Clinical Science* [*Clin. Sci.*] **12**, 41–55, 1953. 6 figs., 28 refs.

In a study of the effects of cortisone and ACTH on experimentally induced inflammatory reactions of the skin carried out at St. Mary's Hospital Medical School and the Statistical Research Unit of the Medical Research Council, London, 13 subjects suffering from diseases known to respond to corticosteroids were used. The agents employed were: purified protein derivative of tuberculin (P.P.D.) and manganese butyrate by intradermal injection; histamine, morphine, pollen, and cat scurf by scratch test; and atropine by patch test. Tests were performed before, during, and at various times after treatment with ACTH and cortisone. Repeated tests were made, and results were assayed by accurate measurement of flare and induration diameter and then subjected to strict statistical analysis.

Erythema and induration response to P.P.D. was significantly reduced during hormone treatment, returning towards pre-treatment levels after cessation of therapy. Reactivity to P.P.D. was reduced between 15- and 170-fold as a result of treatment. The findings for manganese butyrate were similar but rather more variable, and reduction in reactivity was much less. Changes with histamine, morphine, pollen, and cat scurf were not considered statistically significant. Inflammatory response and itching following atropine patch-testing in sensitive subjects were abolished during cortisone treatment. The immediate or histamine reaction did not appear to be influenced by these hormones, but the more delayed type induced by P.P.D. and manganese butyrate was significantly reduced.

[These results, having been subjected to careful statistical study, appear to have established the inhibitory action of cortisone on the tuberculin response beyond reasonable doubt. The reader is referred to the original article for details of experimental technique and statistical methods.] *J. N. Harris-Jones*

495. **Lack of Cortisone Effect in the Early Stages of Inflammation and Repair**
R. LATTES, J. W. BLUNT, H. M. ROSE, R. A. JESSAR, DE G. VAILLANCOURT, and C. RAGAN. *American Journal of Pathology* [*Amer. J. Path.*] **29**, 1–19, Jan–Feb., 1953. 20 figs., 8 refs.

The Rheumatic Diseases

496. **Combined Treatment with Gold and Hormones in Rheumatoid Arthritis.** (Association chryso-hormonale dans la P.C.E.)
F. COSTE, J. CAYLA, F. DELBARRE, and B. PIGUET. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **20**, 1–5, Jan., 1953.

The influence of ACTH (corticotrophin) and cortisone on chrysotherapy was studied in 81 cases of rheumatoid arthritis at the Rheumatological Clinic, Faculty of Medicine, Paris. The cases were divided into three groups: (1) 23 patients who developed signs of intolerance to gold; (2) 40 patients who showed no signs of intolerance; and (3) 18 patients who had received no previous gold treatment.

The results showed that in Group 1, 16 patients were able to tolerate and benefit from combined hormone and gold therapy, but in most cases the effect was transient and reactions occurred after cessation of hormone therapy; in Group 2, 12 patients developed signs of intolerance to gold during or after treatment with hormones; in Group 3, 5 patients showed signs of intolerance during or after hormone therapy. The authors conclude that combined hormone and chrysotherapy gives reasonably good results in the treatment of rheumatoid arthritis in that remissions are induced in about 50% of cases provided that chrysotherapy is started before, or at the same time as, the hormone therapy, but that treatment with gold is useless after hormone therapy.

Kathleen M. Lawther

497. **Phenylbutazone (Butazolidine) in the Treatment of Chronic Arthritis**
L. CUDKOWICZ and J. H. JACOBS. *Lancet* [*Lancet*] **1**, 223–224, Jan. 31, 1953. 4 refs.

The authors report their results in a series of 50 patients with chronic arthritis treated with phenylbutazone at St. Stephen's Hospital, London. Of 34 patients with rheumatoid arthritis, objective improvement was noted in 20, no change in 12, and 2 were worse; 19 patients experienced some subjective improvement. There was no consistent change in the erythrocyte sedimentation rate. Of 3 patients with ankylosing spondylitis, only one was improved both objectively and subjectively, while of 11 patients suffering from osteo-arthritis, 7 were improved objectively, the other 4 remaining unchanged. Side-effects occurred in 22 patients, and varied from abscesses at the site of injection to rashes. The commonest effects were gastro-intestinal symptoms and oedema, but a more serious one was massive melaena, which occurred in 2 patients.

Discussing their findings, the authors suggest that the effect of phenylbutazone is mainly analgesic and not in any way similar to that produced by ACTH. They consider that the high incidence of toxic reactions necessitates careful supervision of the patients receiving this drug, but that nevertheless phenylbutazone has a place in the management of chronic joint disease.

[Unfortunately very little information about dosage is given in this paper beyond the statement that this never exceeded 1 g. per day and that the maximum total dose given was 73 g.]. *William Tegner*

498. **Phenylbutazone in the Treatment of Rheumatism.** (La butazolidina nella terapia antireumatica)
T. LUCHERINI and E. CECCHI. *Minerva medica* [*Minerva med. (Torino)*] **44**, 267–271, Feb. 3, 1953. 23 refs.

499. **Deaths of Two Patients Treated by Phenylbutazone**
J. G. BENSTEAD. *British Medical Journal* [*Brit. med. J.*] **1**, 711–712, March 28, 1953. 3 refs.

500. **A New Reaction for Rheumatic Diseases.** [In English]
E. J. JOKINEN. *Annales medicinae experimentalis et biologiae Fenniae* [*Ann. Med. exp. Biol. Fenn.*] **31**, 54–62, 1953. 10 refs.

In this paper from the University of Helsinki is described a serological test for use in the diagnosis of rheumatic affections, slightly modified from the author's original technique published in 1952. The method consists in measuring 0·25 ml. of serum, drop by drop, into 2·5 ml. of 94% ethanol at room temperature and refrigerating overnight; then centrifuging at 2,500 revolutions per minute for 5 minutes and draining. The precipitate is covered by 1 ml. of 95% sulphuric acid and examined after 5 minutes. The reaction is regarded as positive if all the precipitate dissolves and forms a dark brown solution; as slightly positive if there is partial dissolution with some brown colour; and as negative if there is no dissolution and no colour production.

The method was used for testing 4 groups of sera: Group 1 from 28 patients with rheumatoid arthritis; Group 2 from 14 patients with rheumatic fever; and Group 3 from 129 healthy blood donors. Group 4 consisted of 1,263 samples of serum from the serological laboratories originally taken for routine testing from patients without rheumatic disease. In the first 3 groups the sera were tested at least 4 times each and an average reading taken. From the 28 cases of rheumatoid arthritis 21 (75%) positive results were obtained, and from the 14 cases of rheumatic fever 9 (64%). Positive results were associated with a high erythrocyte sedimentation rate and a high temperature. Of the 9 cases of rheumatic fever giving a positive reaction, 4 out of 5 examined radiologically showed joint changes caused by arthritis. [No further details of this very unusual finding are given.] Treatment with salicylates made no difference either *in vivo* or *in vitro*. No positive results were obtained from the group of healthy subjects. Sera from patients with miscellaneous diseases were also

tested, and these gave varying proportions of positive results, the highest percentage being obtained in liver and collagen diseases and in some cases of carcinoma and of tuberculosis.

It is concluded that in the rheumatic diseases the result of the test depends upon the activity or otherwise of the process, but that the method is not specific for these diseases. *E. G. L. Bywaters*

501. **The Nature, Pathogenesis, and Classification of the Rheumatic Diseases.** (Begriffsbestimmung, Pathogenese und Systematik der rheumatischen Erkrankungen)
W. MOLL. *Praxis* [*Praxis*] **42**, 178–183, March 5, 1953. 32 refs.

502. **A Long-term Survey of Rheumatic and Non-rheumatic Families. With Particular Reference to Environment and Heredity**
F. G. GRAY, R. W. QUINN, and J. P. QUINN. *American Journal of Medicine* [*Amer. J. Med.*] **13**, 400–412, Oct., 1952. 7 figs., 23 refs.

With the object of studying the familial spread of rheumatic disease, two contrasting groups of families have been kept under observation at Yale University School of Medicine for periods of 13 to 23 years. The groups had this in common—that the contact or index member of each family had been a patient at the New Haven Hospital, Connecticut, at some time during the years 1929–39. But whereas the contact members of the larger group, numbering 122, had all suffered from rheumatic fever, the contact members of the smaller group, numbering only 35, were non-rheumatic children and " it was not known at the time of selection that any sibling of the contact case had rheumatic fever ". [Presumably this means that, so far as was known, none of the siblings had ever had rheumatic fever.]

Previous communications have been published reporting the results of this study up to 1939. The present report is concerned with the families which were still available for study in the period 1947–9, namely, 40 of the original 122 rheumatic and 21 of the original 35 non-rheumatic families. [The authors seem less concerned about the loss of 68% of the rheumatic families than about the loss of 40% of the non-rheumatic families, in which group, by substitution, the numbers were increased to 30.]

The incidence of new cases of rheumatic fever, rheumatic heart disease, or both, was found to be higher in the rheumatic families than in the controls. In most instances familial spread was according to order of birth from eldest to youngest—even though not all the members were affected—and there was a tendency for successive cases in a family to occur at progressively higher ages.

The authors found many instances in which streptococcal disease preceded the onset of rheumatic fever, and some evidence that " the occurrence of rheumatic fever in the children approximated the pattern of a single autosomal recessive gene except in the mating of two parents with the disease."

In 1930–31, when the incidence of rheumatism was at a peak, the two groups of families were comparable as regards distribution of family size and income level (the income of 90% of both groups being judged too meagre to assure adequate nutrition, clothing, and the basic essentials of family life), but poor housing and overcrowding were significantly more prevalent among the rheumatic families. This leads the authors to speculate whether the inherited factor, if it does exist, may be an altered response to repeated infection, enhanced by the presence of poor housing and overcrowding, rather than an increased susceptibility to rheumatic fever *per se*.

[No indication is given of the method by which the contact members of either group were originally selected. Furthermore, in the absence of evidence to the contrary, it is not unreasonable to suppose that the 40 rheumatic families were the families in the original group in which most of the subsequent cases of rheumatic disease occurred and just for this reason were available for study in 1947–9. The alternative possibility that the findings are explicable in the light of the bias present in such select data cannot therefore be entirely overlooked.]
E. Lewis-Faning

503. **Prophylaxis of Recurrences of Rheumatic Fever with Penicillin Given Orally. Final Report of a Five Year Study**
K. H. KOHN, A. MILZER, and H. MACLEAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 347–351, Jan. 31, 1953. 12 refs.

In this paper are reported the final results of a 5-year study of the effect of oral penicillin in preventing recurrences of rheumatic fever in Chicago school-children. [For an account of the first 3 years' findings, see *J. Amer. med. Ass.*, 1950, **142**, 20; *Abstracts of World Medicine*, 1950, **7**, 657.] During the first 2 years of the study the authors found that the administration of 200,000 units of penicillin 4 times a day for the first week of each month from October to June caused the most satisfactory reduction in the incidence of Group-A β-haemolytic streptococci in throat swabs and in the number of recurrences of rheumatic fever of any of the schedules tried, and this was therefore adhered to for the 3rd, 4th, and 5th years. The total number of recurrences occurring during these three rheumatic-fever seasons in the treated children (totalling 133 patient-seasons) was 2 (1·5%), compared with 26 (16·99%) and 39 (20·21%) in two control groups (153 and 193 patient-seasons respectively). As 50% of all recurrences in Chicago occur between February and March, they suggest that in these months penicillin should be given in alternate weeks, and at other times in the year for one week each month. They do not recommend the use of lozenges, because of the development of stomatitis. They consider that prophylaxis should be continued through puberty and possibly longer. In no case was penicillin resistance found in Group-A haemolytic streptococci. Approximately 50% of the Group-A strains isolated during the 4th and 5th years could not be typed, for which no explanation is offered. *R. S. Illingworth*

Traumatic Surgery and Orthopaedics

504. **The Role of Cold Hemagglutinins in Frostbite**
D. WEINER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **41**, 114–121, Jan., 1953. 47 refs.

According to the literature cold haemagglutination is found with a high degree of frequency only in primary atypical pneumonia and trypanosomiasis, the titre in the former condition rapidly falling during convalescence. It is thought to play a part in certain types of haemolytic anaemia, and may be an important factor in paroxysmal cold haemoglobinuria and in certain cases of Raynaud's syndrome and similar peripheral vascular phenomena; in 2 reported cases of this condition gangrene of the tips of the extremities occurred.

The author, at the U.S. Army Medical Research Laboratory, Fort Knox, Kentucky, carried out an investigation to determine whether there was any association between cold haemagglutination and the incidence of frostbite, the subjects being troops with frostbite invalided home from Korea; healthy servicemen acted as controls. It was found that in 74·8% of the men with frostbite and in 40·2% of the controls cold haemagglutination occurred, the difference between the two groups being more significant when the higher titres were considered. Age was a definite factor, the frequency decreasing with advancing age; haemagglutination was more common in negroes than in the white subjects. Exposure to cold did not appear to alter the titre nor the incidence of the agglutinin.

It is concluded that there is a significant relationship between the presence of cold haemagglutinins and the occurrence of frostbite, in which clumping occurs in the superficial vessels, resulting in a slowing of the blood flow and even occlusion of vessels. Although frostbite is observed in the absence of cold haemagglutinins, their presence is probably an important contributory factor.

Peter Martin

505. **Subacute and Chronic Osteomyelitis. Treatment with Use of Chemotherapeutic Agents, Antibiotics, and Primary Closure ; Follow-up Report**
F. D. DICKSON, R. L. DIVELEY, and R. H. KIENE. *Archives of Surgery* [*Arch. Surg.* (*Chicago*)] **66**, 60–68, Jan., 1953. 3 refs.

In 1941 the authors published a preliminary report (*J. Bone Jt Surg.*, **23**, 516) on the treatment of 21 cases of subacute and chronic osteomyelitis by thorough debridement followed by administration, locally and systemically, of sulphathiazole and primary closure of the wound. In the present paper, from the Dickson–Diveley Clinic, Kansas City, they describe 104 cases in which 140 operations were carried out, different sulphonamides and penicillin being given systemically.

The operation was performed under a tourniquet. Methylene blue was used to stain all necrotic tissue, which was carefully removed by dissection, and all rough edges of bone smoothed with an electric burr. Thorough irrigation of the wound with normal saline was followed by deep suture and obliteration of all dead space by muscle grafts. Sulphathiazole powder, 0·5 to 1 g., was lightly insufflated into the wound in layers, and a plaster-of-Paris cast applied after the wound had been closed by interrupted cotton sutures. The authors recommend the application of a voluminous firm dressing under the plaster, which is left in position for 3 weeks.

Sulphathiazole was applied locally in all cases, but for purposes of systemic treatment the cases were divided into 3 groups, receiving sulphathiazole, sulphadiazine, and penicillin respectively. Healing was by primary intention in 117 of the 140 operations, but little difference was observed between the results in the three groups; the authors attribute this to the effectiveness of the local application of sulphathiazole. Staphylococcal toxoid is recommended as a useful adjuvant treatment which prevents recurrence of infection in some cases.

Eric. I. Lloyd

506. **A Case of Osteomyelitis of All the Small Bones of the Hands and Feet**
M. D. BABER. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **28**, 24–25, Feb., 1953. 4 figs., 3 refs.

TRAUMATIC SURGERY

507. **Effect of Vitamin C Deficiency on Healed Wounds**
C. L. PIRANI and S. M. LEVENSON. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **82**, 95–99, Jan., 1953. 6 figs., 19 refs.

At the U.S. Army Medical Nutrition Laboratory, Chicago, the authors have studied the effects of changing from a nutritionally complete diet to one lacking ascorbic acid on healed laparotomy scars, 6 weeks old, in young male guinea-pigs. Clinical signs of scurvy were present in all these animals at the end of the third week after change of diet, and they were killed on the 26th day. During the last few days of life the abdominal scars, which had been barely visible, showed swelling and small haemorrhages and, in some cases, herniation. Histologically the epidermis was intact, as was a thin layer of the immediately subjacent connective tissue. Elsewhere the connective tissue of the scar was loose and more cellular than it appeared in the scars of control animals, while the collagen fibres were stained poorly by van Gieson's technique. Frank granulation tissue was present and contained defective capillaries with related small haemorrhages. The changes were confined to the scar tissue, which thus appears to be more sensitive to lack of ascorbic acid than normal connective tissue.

K. G. Lowe

508. **The Use of Tracheotomy in the Treatment of Crushing Injuries of the Chest**

B. N. CARTER and J. GIUSEFFI. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **96**, 55–64, Jan., 1953. 3 figs., 3 refs.

Tracheotomy has been performed by the authors since 1949 at Cincinnati General Hospital as a primary form of treatment for crushing injuries of the chest. It is pointed out that such injuries lead to paradoxical movement of the chest wall on respiration, severe pain on movement, and copious tracheo-bronchial secretion, all of which produce unsatisfactory aeration of the lung. Tracheotomy reduces the paradoxical chest movement, alleviates pain, and provides an easy method of aspiration of the bronchial secretion. In addition, as a result of tracheotomy there is a reduction in the volume of dead space (mouth, pharynx, and nasal passages) and a decrease in the resistance to respiration, both being factors which play an important part in improving respiratory function.

The authors describe 11 cases in which the uses and value of this procedure are exemplified. Several of the patients would undoubtedly have died had not tracheotomy been performed: in some cases the clinical response was remarkably rapid. It is emphasized that certain precautions are necessary in the management of patients with a tracheotomy: (1) as patients are unable to cough the trachea must be carefully aspirated at suitable intervals; (2) aspiration should be carried out with great care and suction used for short periods, since it is possible to produce rapid and severe anoxia, with resultant stimulation of the vasovagal reflexes and cardiac arrest. *W. P. Cleland*

509. **Supportive Therapy. An Improved Type of Dextran**

A. M. BOYD, F. FLETCHER, and A. H. RATCLIFFE. *Lancet* [*Lancet*] **1**, 59–63, Jan. 10, 1953. 5 figs., 8 refs.

An efficient plasma substitute (or " blood-volume restorer " which the authors suggest as a more appropriate name) must fulfil the following criteria: (1) ease of administration in all climates; (2) freedom from undesirable side-effects; (3) its manufacture on a large scale must be easy and economic, and the composition of the product readily standardized; (4) the material must be storable without alteration for long periods; (5) after injection it should eventually be excreted or metabolized, yet 24 hours after the end of the infusion at least 50% of the amount infused should still be in the circulation. The type of dextran at present in use adequately fulfils most of these criteria, but its rate of excretion depends on the range of the molecular weights of the partially hydrolysed dextran molecules present, and in this respect standard preparations of dextran are unsatisfactory.

The largest molecule of a polymer of glucose such as dextran which will diffuse through the capillary walls has a molecular weight of about 130,000, while the infusion of molecules whose weight is more than 250,000 is undesirable because of possible sensitization effects. The ideal blood-volume restorer should therefore have a molecular-weight range between 130,000 and 250,000. By intensive fractionation several " narrow-fraction " dextrans were prepared at the University of Manchester, and their " molecular spectrum " calculated from intrinsic-viscosity measurements, that of one fraction (" C ") most nearly approaching the ideal. In human subjects after an infusion of standard dextran the 24-hour excretion rate was 35% and the blood level at the end of 24 hours was 20% of the level on completion of the infusion, whereas when narrow-fraction dextran C was infused the values were 8% and 68% respectively.

Narrow-fraction dextran (" dextraven ") has been used in 120 cases at Manchester Royal Infirmary and associated hospitals for the prophylaxis or treatment of surgical shock. For the former purpose, unless there was excessive haemorrhage, the infusion of narrow-fraction dextran during the operation was sufficient to maintain the blood-pressure and circulating blood volume, postoperative infusion usually not being necessary, so that the quantity of fluid given was not large enough to cause any significant degree of haemodilution. In the treatment of shock most cases responded satisfactorily to the infusion of 2 bottles (about 1 litre) of narrow-fraction dextran, care being taken to avoid excessive haemodilution by giving blood in addition to dextran in cases requiring a larger infusion. A number of cases of burns have also been treated, but their number is insufficient to allow any conclusions as to the usefulness of narrow-fraction dextran for this purpose to be reached.

Like other macro-molecular substances, narrow-fraction dextran causes a rise in the erythrocyte sedimentation rate, which is maintained for 3 to 5 days after the infusion, and it may also cause difficulty in the typing and cross-matching of blood. Blood should therefore be taken for this purpose before the infusion is begun. If a muscle relaxant is required during an operation in which narrow-fraction dextran is being used, gallamine (" flaxedil ") is best avoided, since haematoma formation is not uncommon with gallamine even in the absence of supportive therapy, and is made more likely if the blood pressure is maintained during operation by dextran infusion. " Tubarine " was used without haematoma formation. A mild rigor in one case is the only reaction which has so far been reported after infusion of narrow-fraction dextran. *P. Mestitz*

510. **The Early Treatment of Burns at a Regional Plastic Centre. With a Review of 100 Cases Treated by Exposure**

A. J. EVANS. *British Journal of Plastic Surgery* [*Brit. J. plast. Surg.*] **5**, 263–274, Jan., 1953. 6 figs., 7 refs.

The author describes the salient points in the management of 100 cases of fresh burns (admitted within 72 hours) treated at Parle Prewett Hospital, Basingstoke, Hampshire, over the past 2 years. In his unit dextran has entirely replaced plasma for intravenous therapy, but in the presence of severe full-thickness loss of skin, blood is given early and generously during the shock stage. Once the patient is over this, gentle cleansing is carried out in the ward without anaesthesia, and a repeated

frosting of penicillin powder used to assist drying. It has sometimes proved difficult to keep the burned area clear of bedclothes, and small areas of moist pressure have had to be accepted, though there has been little impairment of the main result. Nearly 60 of these burns healed under their crust, and the aim in all the other cases has been to apply grafts between the 8th and 15th days. Earlier excision and grafting is deprecated as putting an unfair strain on the metabolic balance of a patient with a severe injury, and immediate excision is reserved for the localized deep burn which is common only in industrial areas. Sloughs were expeditiously shaved off with a Humby knife, and the Brown electric dermatome has made it possible to take razor grafts quickly even from awkward donor sites. These have mostly been applied as sheets and sutured into place whenever this could be done. Only occasionally has it been possible to leave the grafts exposed, the majority being covered with the standard pressure dressing. Where it was necessary to make repeated use of the same donor site, satisfactory grafts were obtainable after 3 weeks; homografts were used only as a temporary expedient in a few cases of very extensive burns.

Nearly half the total cases were in children under 5 years, but in 80 patients the injury involved less than 20% of the body surface. The average stay in hospital was 32 days. The 8 deaths in the series occurred at all ages; they had no factor in common except the severity of the burn. *R. P. G. Sandon*

PHYSICAL MEDICINE

511. **Effect of Various Procedures on the Flow of Lymph**
E. C. Elkins, J. F. Herrick, J. H. Grindlay, F. C. Mann, and R. E. De Forest. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **34**, 31–39, Jan., 1953. 9 figs., 12 refs.

The exact mechanism of the lymph flow is uncertain, but it has been definitely established that exercise and massage produce an increase in the rate of flow. The effect of various forms of heat therapy on the rate is, however, still controversial, and consequently a study of this in dogs and rats was made by the authors at the Mayo Clinic. A cannula was inserted into the thoracic duct of 10 dogs in order to collect all the lymph from below the diaphragm. The normal flow was measured over several days, after which various heating agents were applied to the clipped hindquarters, the flow rate being measured during and after treatment. The heating agents used were: infrared radiation emanating from a source at 12 inches (30·5 cm.) distance, short-wave diathermy using an induction cable, microwave diathermy with the director at 2 inches (5·1 cm.) distance and an output of 65 or 93·5 watts, and hyperpyrexia produced by a humidified heated chamber around the dog's head. The period of heating was approximately 30 minutes, but the temperature was recorded only in certain cases. Anaesthesia was often necessary to keep the dogs quiet and so eliminate the effects of exertion on the flow of lymph.

The results showed clearly that none of these heating agents produced any significant alteration in the rate of flow of lymph. As a control, exercise or massage were introduced under similar circumstances and produced a marked increase in the rate. Some of the dogs developed a hypoproteinaemic oedema of the hind legs and were treated by kneading and stroking massage, which resulted in a marked increase in the lymph-flow rate and a decrease of the oedema, while in one dog which died, passive exercise after death caused a similar increase in the flow rate. In similar experiments with rats similar results were obtained; in some instances the flow of lymph even seemed to decrease during hyperthermia.
M. H. L. Desmarais

512. **A Critical Evaluation of Treatment of Traumatic Effusions of the Knee**
J. B. Millard and C. B. Wynn-Parry. *Annals of Physical Medicine* [*Ann. phys. Med.*] **1**, 156–162, Jan., 1953. 2 figs., 3 refs.

An investigation was carried out at three R.A.F. Medical Rehabilitation Units to determine the best method of accelerating the disappearance of an effusion from the knee. The 260 patients were all young men; in 91% the effusion followed meniscectomy and in the remainder the cause was traumatic. Cases in which the effusion was associated with any pathological condition, such as torn cartilage, loose bodies, or arthritis, were excluded. The patients were divided into 6 groups, all of which carried out intensive quadriceps exercises (knee flexion being prohibited) and remedial games, and certain additional measures, the nature of which differed from group to group, were applied. These are given below, with the average time taken for the effusion to disappear:

(1) Crepe bandage worn day and night	23·0 days
(2) Daily " through-and-through " constant-current galvanism	24·8 ,,
(3) Back-splint and bandage, day and night	9·9 ,,
(4) Back-splint, bandage, and daily anodal galvanism	14·2 ,,
(5) Confined to bed, with back-splint and bandage	9·4 ,,
(6) No additional treatment	23·3 ,,

The back-splint used was a light metal splint applied posteriorly and extending from mid-calf to mid-thigh: it was worn continuously, day and night, not even being removed for exercise or games periods.

The authors emphasize that both electrotherapeutic techniques (details of which are given in the text) were carried out meticulously, but in spite of this, their ineffectiveness in this investigation is apparent. The crepe-bandage support did not appear to accelerate the disappearance of an effusion, but the use of a back-splint appeared to be of considerable value in this respect, no further significant improvement being obtained by the addition of rest in bed. Absolute immobilization of the knee, therefore, appears to be the most important measure in the treatment of these effusions, but this must be accompanied by intensive quadriceps exercises if recurrence is to be avoided. *B. E. W. Mace*

Neurology and Neurosurgery

513. **Acute Disseminated Encephalomyelitis Treated with A.C.T.H.**
H. G. MILLER. *British Medical Journal* [*Brit. med. J.*] **1**, 177–183, Jan. 24, 1953. 14 refs.

The author first discusses the action of cortisone and ACTH in " allergic " disorders of the nervous system and then describes 7 cases, seen at the Royal Victoria Infirmary, Newcastle-upon-Tyne, in which a diagnosis of " acute disseminated encephalomyelitis " was made and in which ACTH was administered. All the patients were said to be deteriorating up to the time ACTH therapy was started. No extravagant claims are made for this treatment, it being suggested only that ACTH should be given a further trial in similar patients. The ages of the patients varied from 6 to 30 years. In 2 the neurological syndrome was a complication of varicella. [In view of the known natural history of this complication it would be unwise to draw any conclusions.] The diagnosis in 2 more cases was " transverse myelitis " and " severe ascending myelitis " respectively, but there was no evidence of brain involvement in either. In 2 further cases the patients were brothers, one of whom had had several similar cerebral illnesses. In only 2 cases was there an increase in cells in the cerebrospinal fluid.

[There is little evidence that the condition in these patients constituted a single syndrome, let alone a " disease ", nor is there much evidence that it was inflammatory. Since the brain was not always involved, the term " acute encephalomyelitis " would seem to be inappropriate.] *Hugh Garland*

514. **Neurological Complications following Antirabies Vaccination**
E. APPELBAUM, M. GREENBERG, and J. NELSON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 188–191, Jan. 17, 1953. 12 refs.

The occurrence of encephalomyelitis in 46 patients vaccinated with phenolized rabies virus in New York City between 1928 and 1951 is reported. There were no fatalities, so that the morbid anatomy could not be studied, but in reports of other series a disseminated encephalomyelitis has been described, with perivascular lymphocytic infiltration, proliferation of microglia, and partial demyelination with relative sparing of the nerve cells, while changes have also been described in the nerve roots and peripheral nerves. In the present series the clinical manifestations enabled the cases to be divided into encephalitic, myelitic, and neuritic types. The onset of neurological complications occurred some days after the first injection, chiefly between the 8th and 21st days (with extremes of 6 and 45 days). The onset was usually sudden with headache and vomiting. Examination of the cerebrospinal fluid generally showed a considerable increase in the number of leucocytes, usually mostly lymphocytes though sometimes polymorphonuclear leucocytes predominated; there was also a moderate rise in protein content. The over-all incidence of this complication was one in every 2,025 persons treated, but it was five times higher in those patients who were given 14 injections of the vaccine than in those who received 7 or less. Since it is estimated that rabies develops in 5 to 15% of persons bitten by a rabid animal, the risk of neurological complications from vaccination is considerably less than that of withholding treatment.
Hugh Garland

515. **Acute Respiratory Failure in Multiple Sclerosis and its Management**
T. C. GUTHRIE, J. F. KURTZKE, and L. BERLIN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **37**, 1197–1203, Dec., 1952. 6 refs.

The authors report, from the Veterans Administration Hospital, Bronx, New York, 4 cases of multiple sclerosis in which acute ventilatory failure occurred during an exacerbation of the disease. This was associated with the development of a quadriplegia and, in 3 of the patients, with a sensory loss up to the cervical or upper thoracic level. The bulbar functions were not impaired. The patients were treated in a respirator. Two survived and made a good recovery and 2 died.

The authors believe that acute respiratory failure due to paralysis of the muscles of respiration is probably the cause of death in many of the fatalities associated with acute episodes of multiple sclerosis and urge that if these cases were treated in respirators some of the deaths might be avoided. They also recommend that preparations for the performance of emergency bronchoscopy and tracheotomy should be made. *N. S. Alcock*

BRAIN AND MENINGES

516. **Intracranial Hypotension**
F. PAGE. *Lancet* [*Lancet*] **1**, 1–5, Jan. 3, 1953. 29 refs.

The influence of abnormally low intracranial pressure on neurological symptoms has been studied by the author at the Middlesex Hospital, London. The symptoms are not specific in type and resemble those seen in cases of raised intracranial pressure. The author points out that cerebral hypotension occurs: (1) after lumbar puncture and spinal analgesia; (2) following closed or open head injuries with or without loss of cerebrospinal fluid (C.S.F.) from the ear; (3) after cranial operations; and (4) in unrelated medical and neurological disorders. He discusses the possible pathogenesis in cases in the second group, where there is no leakage of C.S.F., and suggests that diminished cerebral blood flow may be important in the causation of intracranial hypotension. In mild cases treatment consists in raising the

foot of the bed and forcing fluids by the mouth; in severe cases 20 to 40 ml. of distilled water should be given intravenously, or 20 to 25 ml. of physiological saline by lumbar puncture.

[The subject of intracranial hypotension has received considerable attention in France but has been somewhat neglected in Great Britain. This paper, with 4 illustrative cases, is of considerable interest.]

J. W. Aldren Turner

517. **Hallucinations due to Prefrontal Lesions and their Interpretation.** (Les hallucinations dans la pathologie préfrontale. Essaie d'interprétation)

R. MESSIMY. *Presse Médicale* [*Presse méd.*] **61**, 52–54, Jan. 14, 1953. Bibliography

True hallucinations are characteristically accompanied by a firm conviction of their reality—so much so that they may be terrifying—and are to be distinguished from the sensory phenomena (illusions, hallucinoses) accompanying certain lesions of the cortex in which insight is retained. Hallucinations associated with prefrontal lesions are rarely simple in character; as a rule they show two or more components which may be visual, auditory, olfactory, or cœnaesthetic.

The case is described of a patient who had sustained bilateral orbito-frontal trauma from a gunshot wound, and who believed that he had given birth to many children and animals through his head. These he claimed to be able to feel and recognize, though he was unable to see them. Later he developed complex auditory and olfactory hallucinations of savage animals. Such hallucinations are regarded as typical of prefrontal lesions. Psychotic illnesses are frequently accompanied by similar hallucinations, and as the resemblance to those resulting from prefrontal lesions is close, it is suggested that they have a common origin. The author also argues that hallucinations should be regarded as positive release phenomena in the Jacksonian sense—as should the other signs resulting from prefrontal lesions—and as the product of subcortical mechanisms.

[The interesting speculations and close reasoning of this paper, with its many references to the appropriate literature, are not readily summarized, and the paper itself should be read by those interested in the nature of hallucinations.] *L. G. Kiloh*

518. **Mesencephalotomy in Treatment of "Intractable" Facial Pain**

E. A. SPIEGEL and H. T. WYCIS. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **69**, 1–13, Jan., 1953. 8 figs., 8 refs.

The authors (who are pioneers of the method of producing electrolytic lesions at precise points in the less accessible parts of the brain by means of a stereotaxic apparatus, the stereoencephalotome) report the treatment at Temple University Hospital, Philadelphia, of 6 cases of intractable facial pain by the production of lesions of the pain-conducting pathways in the mid-brain (mesencephalotomy). In 3 of the cases this was combined with the production of electrolytic lesions in the dorsomedial nucleus of the thalamus, with the object of reducing the emotional reactivity to any remaining pain transmitted by accessory pain-conducting fibres.

In 3 of the cases the diagnosis was of tic douloureux, for which retrogasserian rhizotomy had already been carried out without relief; the fourth case was one of thalamic pain, which cortical ablation had failed to improve; in the fifth case the pain was of pontine origin and had persisted after contralateral prefrontal leucotomy; and the sixth case was of post-herpetic neuralgia unrelieved by retrogasserian rhizotomy. Relief of pain for the duration of observation was obtained in one of the cases of tic douloureux (4½ years) and in the case of pontine pain (9 months); in one other case of tic douloureux a transitory relapse occurred after over 3 years' relief, but the patient with thalamic pain was relieved for only 4½ months, probably owing to incomplete interruption of the pain-conducting systems; this last case at least demonstrates the important part played by afferent impulses in the pathogenesis of thalamic pain. In the remaining 2 cases the post-operative period was too short to permit any appraisal of results. Complications of the procedure were mostly transient and did not appear to be serious, at least in comparison with the relief of pain which resulted from it.

J. V. Crawford

519. **The Results of Superior Cervical Sympathectomy and Carotid Jugular Anastomosis in Atrophy of the Brain**

A. STOWELL and R. A. HAYNE. *Southern Medical Journal* [*Sth. med. J.* (*Bgham, Ala.*)] **45**, 1145–1151, Dec., 1952. 5 figs., 6 refs.

In this paper from the Springer Clinic, Tulsa, Oklahoma, the authors, after reviewing the salient features of the syndrome of brain atrophy in patients under 45 years of age, present the results of surgical treatment in 109 cases.

They find that such cases fall into two main groups, the adults showing signs and symptoms of brain tumour without increased intracranial pressure, and the children presenting as cases of cerebral palsy with or without marked mental involvement. The types of atrophy encountered were divided, on pneumoencephalographic evidence, into: (1) cerebral atrophy with enlarged ventricles; (2) atrophy with increased subarachnoid space; (3) cortico-cerebral atrophy; (4) cortico-cerebellar atrophy with enlarged sulci and increased subarachnoid space in the posterior fossa; (5) cerebro-cerebellar atrophy; and (6) diffuse brain atrophy.

In 44 of the 109 patients, mainly adults, superior cervical ganglionectomy was performed; the other 65 cases were treated by carotid–jugular anastomosis, 12 of them undergoing combined unilateral cervical sympathectomy and carotid–jugular anastomosis. Ligation of one internal jugular vein with bilateral superior cervical sympathectomy was performed in 4 later cases. There was no mortality or morbidity in the whole series. After cervical sympathectomy 19 cases showed definite improvement and 15 slight or moderate improvement as judged by the clinical neurological disability. The remaining 10 cases were not improved and, in fact, continued to deteriorate.

The 65 patients, mostly children, in whom carotid–jugular anastomosis was performed were divided into two groups according to whether or not they had epilepsy. Of the 25 cases with intractable epilepsy approximately 30% improved, 2 patients remaining free from fits for 2 years after operation. In 12% of the children and 32% of the adults in the non-epileptic group objective reduction of weakness or ataxia was noted, but in the remainder there was no improvement. In only 4 of the 65 cases was there appreciable improvement in the intelligence quotient following operation. The authors therefore feel that, apart from the possible use of jugular–carotid anastomosis in cases of intractable epilepsy, this procedure should not be used except as an experimental method. *J. V. Crawford*

520. **The Effects of Occlusion of the Anterior Inferior Cerebellar Artery**
W. J. ATKINSON. *Annals of the Royal College of Surgeons of England* [*Ann. roy. Coll. Surg. Engl.*] **12**, 126–135, Feb., 1953. 3 figs., 2 refs.

521. **Traumatic Internal Carotid Artery Thrombosis Secondary to Nonpenetrating Injuries to the Neck. A Problem in the Diagnosis of Craniocerebral Trauma**
R. C. SCHNEIDER and L. J. LEMMEN. *Journal of Neurosurgery* [*J. Neurosurg.*] **9**, 495–507, Sept., 1952. 7 figs., 34 refs.

The authors review 5 previous cases reported in the literature in which thrombosis of the internal carotid artery caused by trauma has mimicked an intracerebral lesion, and describe 2 cases of their own seen at the University of Michigan Hospital, Ann Arbor. The first patient, a woman of 49, was thrown out of a motor-car and struck the right side of her head. It was not known if loss of consciousness had occurred, but she became progressively lethargic after admission to hospital. There were abrasions on the right side of the head, in the right supraclavicular region, and in the chest, and within 12 hours of injury she had developed a complete left hemiplegia. Measurement of the retinal arterial pressure showed it to be 40/25 mm. Hg in the right eye and 115/65 mm. Hg in the left. A left stellate-ganglion block was performed with procaine but made no difference to the hemiplegia. The next day open arteriography was performed which demonstrated a complete block of the right internal carotid artery 3 cm. distal to its origin. There was some improvement following a superior cervical sympathectomy, but 3 months later the patient still had a left hemiplegia with left extensor plantar reflex and homonymous hemianopia, and showed marked emotional lability. In arriving at the diagnosis of arterial thrombosis the authors were guided by the relatively slight impairment of the mental state as compared with the severity of the neurological disability, and they emphasize that in this respect the condition differs markedly from the effects of intracranial haemorrhage.

The second patient, a male aged 24, was also injured in an automobile accident, sustaining multiple abrasions of the right side of the neck, face, and forehead. He was semiconscious when first seen, and during the next 36 hours developed a left hemiplegia and deep coma, with signs of a tentorial pressure cone. The right femur was fractured. Cranial burr-holes failed to reveal blood clot, but the intracranial pressure was greatly increased. Ventriculography showed a marked shift of the ventricles to the left, and on arteriography a complete block of the right internal carotid artery 3 cm. above its origin was found, although no difference between the carotid pulses in the neck had been detected. Bilateral subtemporal decompression and a cervical sympathetic block with lignocaine were performed, but the patient died 24 hours later.

It is pointed out that arteriography is the only certain way of establishing the diagnosis, and it is recommended that the angiogram should include the bifurcation of the carotid and, in the case of percutaneous injection, the tip of the needle too, so that failure to fill the internal carotid due to faulty technique can be excluded. In view of the occurrence of raised intracranial pressure as a result of internal carotid arterial blockage, burr-holes will usually be required to exclude a concomitant intracranial haemorrhage. *Donald McDonald*

522. **Histamine Therapy in Acute Ischemia of the Brain**
A. R. FURMANSKI. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **69**, 104–117, Jan., 1953. 21 refs.

In a previous paper by the same author (*Arch. Neurol. Psychiat.* (*Chicago*), 1950, **63**, 415; *Abstracts of World Medicine*, 1950, **8**, 302) the treatment of acute cerebral ischaemia by the prolonged administration of histamine by intravenous drip infusion was described. The results of this method of treatment in a further 50 cases are now reported. The importance is stressed of the early diagnosis of the presence of ischaemia and of the institution of treatment as soon as possible. Lumbar puncture was usually necessary to differentiate severe ischaemia from gross cerebral haemorrhage or cerebral oedema, and all patients whose cerebrospinal-fluid pressure was over 300 mm. H_2O were excluded from this series. The vehicle for the histamine was 5% dextrose in isotonic saline, the dextrose being omitted in cases of diabetes and the saline in cases of hypertension if the patient was under salt-restriction therapy. The concentration of histamine used was 5·5 mg. of the phosphate per litre. With a standard drip regulator, the rate of administration was begun at 20 drops per minute, which should produce a satisfactory dilatation in the most sensitive patients. If no facial flush was observed in 2 to 3 minutes the speed was increased gradually in steps of 5 or 10 drops per minute until flushing occurred. The correct speed was noted for future infusions, as it was relatively constant in the same subject. A rate of 80 drops per minute was seldom exceeded. The infusion was given for 4 to 6 hours and repeated twice daily until improvement had been maintained for 2 or 3 days. The treatment was usually stopped after 2 weeks if no improvement was obtained.

Of the 50 patients, 30 were considered to show an improvement of over 75% (assessed according to a

system of qualitative and quantitative " units of dysfunction ") and 8 patients an improvement of 40 to 60%. The factors which appeared to exert a favourable influence were a mild degree of neurological dysfunction, absence of stupor or coma, absence of cardiac insufficiency, the patient's age being under 60, and short duration of symptoms.

[The author admits the desirability of determining whether the improvement noted was significantly greater than would have been obtained without histamine, but provides no answer—owing, he states, to the difficulty of obtaining comparable study and control groups. This difficulty would not appear to be insurmountable, and adequate controls are a necessary prerequisite for the acceptance of any conclusions concerning the effects of treatment in conditions such as this.]

J. MacD. Holmes

523. **The Aneurysmal Origin of Non-fatal Subarachnoid Haemorrhage. An Angiographic Survey of 53 Cases**
W. B. HAMBY. *Journal of Neurosurgery* [*J. Neurosurg.*] **10**, 35–37, Jan., 1953. 3 refs.

In an earlier paper (*J. Amer. med. Ass.*, 1948, **136**, 522; *Abstracts of World Medicine*, 1948, **4**, 649) the author reported that in a series of 47 patients in which the cause of spontaneous subarachnoid haemorrhage was discovered at operation or necropsy this proved to be an aneurysm in 44 cases (93·6%). In the present paper from Buffalo General Hospital (University of Buffalo) he reports the result of angiographic investigation of 53 cases of spontaneous subarachnoid haemorrhage. In 22 (41%) of the cases the presence of an aneurysm was revealed by this method.

The author points out that aneurysms can thus be demonstrated in a high proportion of non-fatal cases of subarachnoid haemorrhage, as well as of fatal cases. He stresses the fact that complete visualization of the intracranial vascular tree is necessary to disclose the largest possible number of aneurysms, and emphasizes that in this respect his own cases were incompletely investigated. Nevertheless, even injection of both carotid arteries and one vertebral artery may fail to reveal some aneurysms, and the author believes that those arising from the anterior communicating artery are missed particularly frequently. He concludes, however, that in spite of its shortcomings " angiography is the best adjuvant available at present for identification of the lesions responsible for subarachnoid haemorrhage."

J. E. A. O'Connell

524. **Problems Related to Treatment of Intracranial Aneurysms by Carotid Ligation**
R. R. J. STROBOS and L. A. MOUNT. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. (Chicago)*] **69**, 118–128, Jan., 1953. 2 figs., 17 refs.

The different results that theoretically may follow carotid ligation in the treatment of intracranial aneurysms are discussed. The paucity of sufficient follow-up data and the necessity of extensive statistical studies are stressed. For the purpose of establishing criteria for the prediction of the outcome of carotid ligation, 14 patients were studied by means of pressure recordings from the internal carotid artery, preceding and after occlusion of the different carotid arteries, as well as by arteriography with compression of the contralateral internal carotid artery. This study seemed to indicate that when the anterior collateral circulation through the circle of Willis was found to be deficient with arteriography, the mean pressure in the internal carotid artery showed a fall of 55% or more of the original mean value after occlusion of the internal carotid artery or combined occlusion of the common and external carotid arteries. Most of the complications following carotid ligation, however, occurred in the patients who showed a fall of mean pressure of 65% or more upon the outlined occlusion, or a fall of the systolic pressure of 70% or more of its original value. The reliability of these studies as a means of prophesying complications may, however, be seriously hampered by the occurrence of a fall in the general blood pressure or of local spasm after carotid ligation, and two patients are presented who demonstrate these effects. Use of the Selverstone clamp, which permits quick release of the carotid occlusion, prevented permanent sequelae in those patients who showed complications.

In two patients pressures in a cortical branch of the middle cerebral artery were recorded at the same time as pressures in the internal carotid artery on the same side. Occlusion of the carotid arteries resulted in a fall in pressure in the cortical artery of almost equal degree to that in the internal carotid artery. These records indicate that even the peripheral cortical circulation can be profoundly influenced by carotid ligation.—[Authors' summary.]

525. **Conservative Surgical Treatment of Massive Cystic Lymphangioma**
G. C. FREEMAN. *Annals of Surgery* [*Ann. Surg.*] **137**, 12–17, Jan., 1953. 6 figs., 7 refs.

EPILEPSY

526. **The Treatment of Petit Mal with Methylphenylsuccinimide.** (Le traitement du petit mal par le méthylphényl succinimide)
J. LEREBOULLET, R. PLUVINAGE, L. VIDART, and J. THOMAS. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **69**, 87–92, Jan. 23, 1953. 2 refs.

After briefly reviewing the results reported by Zimmerman (*Arch. Neurol. Psychiat. (Chicago)*, 1951, **66**, 156) and Millichap (*Lancet*, 1952, **2**, 907) [*Abstracts of World Medicine*, 1952, **11**, 188 and 1953, **13**, 321] in the treatment of petit mal with methylphenylsuccinimide (" milontin ") the authors report their own results at the Neurological Clinic of the Hôpital Bicêtre, Paris, in 10 patients with petit mal, of whom 8 were 19 years of age or more, the remaining 2 being aged 15 and 12 years respectively. Most of the patients exhibited grand mal combined with petit mal, and had not been improved while taking the usual oxazolidine compounds. The

histories of the patients and the previous treatment they had received are reported in detail.

The authors' results, assessed after a 7-month trial, were comparable to those of other observers. In 6 of the patients the petit-mal seizures were completely controlled or were reduced in number by more than 75%. The authors comment that the associated grand mal was not aggravated, but rather improved by milontin. [In most instances, however, a barbiturate drug was also given.] Of 9 patients in whom the electroencephalogram was typical of petit mal, only one showed a more stable record following treatment.

With a low dosage of milontin, ranging from 0·9 to 2·1 g. daily, toxic effects were not encountered. Leucopenia, a side-effect common to the oxazolidine compounds, did not develop, and microscopic haematuria, known to occur in children taking large doses of milontin, was not observed in the present series of older patients.

[A new drug must do more than demonstrate a positive effect; it must prove to be superior to drugs of established value. In efficacy, milontin is at least equal to the oxazolidine compounds, troxidone and aloxidone. Its use in preference to the latter seems warranted, since no definite case of leucopenia has yet been reported.]

J. G. Millichap

527. **Personal Experience in the Surgical Treatment of Epilepsy**

S. OBRADOR. *Journal of Neurosurgery* [*J. Neurosurg.*] **10**, 52–63, Jan., 1953. 7 figs., 17 refs.

Of 755 major intracranial operations performed by the author at the Institute of Neurosurgery, Madrid, in the last 5 years, 130 (17%) were undertaken for the treatment of epilepsy, 90 patients being operated upon for expanding intracranial lesions, of which glioma (49 cases) and meningioma (14) were the most common. A quarter of all patients with such lesions suffered from seizures and it is believed that half of the survivors continue to have attacks after operation, although the author has not yet confirmed this from his own material. In 30 cases the epilepsy resulted from a focal lesion, in 11 from a localized scar secondary to head injury or infection, and in 19 from an atrophic lesion. These atrophic cases included 12 patients with cerebral hemiatrophy with associated infantile hemiplegia, 3 cases of porencephalic cyst, and 4 cases of cortical atrophy of unknown aetiology which were explored for suspected neoplasm.

The results of treatment in the 9 cases due to localized scar which could be followed up after operation were good (no more fits) in 5; 1 was improved (number of fits diminished) and 3 unchanged. In 6 of the cases of hemiatrophy which were treated by local excision the results were bad; the 6 other patients were treated by hemispherectomy; 2 died and 4 were improved, but 3 of these continued to have attacks. The other patients with atrophic lesions were not benefited by operation.

In 8 cases with psychomotor attacks and in 2 other cases the attacks of epilepsy could not be associated with any demonstrable cerebral lesion. Anterior temporal lobectomy on the side showing the greater electroencephalographic abnormality was considered to have been beneficial in the small group of cases having pure psychomotor attacks; when there were generalized convulsions in addition, however, the results were poor. An attempt to influence the epileptic attacks by making small stereotaxic lesions in the thalamus in 2 patients proved of little value, although one patient obtained some relief.

J. E. A. O'Connell

CRANIAL NERVES

528. **Additional Support for Cajal's Theory Concerning the Crossing of the Nerve Fibres in the Optic Chiasma.** (Más aportaciones a la teoria de Cajal sobre el entrecruzamiento de las fibras nerviosas en el quiasma óptico)

M. MARQUEZ. *Ciencia* [*Ciencia* (*Méx.*)] **12**, 65–70, 1952. 9 figs., 8 refs.

On the occasion of the centenary of Cajal's birth the author, who is a professor in the University of Madrid, reviews the theory whereby Cajal explained the differences in the distribution of fibres in the optic chiasma in various species. In view of the decussation of the motor fibres and in other parts of the sensory system it might be expected that the nerve fibres from the eye would also all cross over to the opposite hemisphere. Although this does occur in certain of the lower animals, in man it is well known not to be the case. Cajal concluded that the unit that must be considered is the visual field. Where the field of each eye is independent of that of the other, as in the laterally directed eyes of such animals as rabbits, complete crossing will occur and thus the left visual field will be perceived by the right cerebral hemisphere. In higher species with binocular vision, however, the visual fields of the two eyes are congruent and so a partial decussation occurs in the chiasma so that the respective halves of the total visual field are represented in the opposite hemispheres. The present author sets out to demonstrate the universality of this theory by considering the distribution of fibres after reversion to a monocular condition.

[The discussion is entirely of a speculative, theoretical nature and no new anatomical facts are given.]

Donald McDonald

529. **Motor Symptoms in Herpes Zoster.** (Motoriske symptomer ved zoster)

E. MOLTKE. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **115**, 82–86, Jan. 15, 1953. 1 fig., 38 refs.

The author reports, from the Rudolph Berg and Bispebjerg Hospitals, Copenhagen, 6 personal cases of herpes zoster with motor symptoms, and reviews the literature on the subject. His own material consisted of 4 cases of zoster in the territory of the trigeminal nerve. one case with the eruption in Hunt's " geniculate zone ", and one involving the lobe of the ear and that area over the angle of the jaw corresponding to the distribution of the great auricular nerve. In all 6 cases there was paralysis of the 3rd, 4th, or 7th cranial nerves, which did not appear to have any correlation with the area involved by the skin lesions: thus, of the 4 cases with eruptions in the trigeminal territory, in 2 there was

ipsilateral facial palsy and in 2 oculomotor paresis, while the remaining 2 patients also had facial palsy. Put another way, 4 cases of facial palsy occurred, with eruptions respectively in the trigeminal zone (2), the auditory meatus, and the territory of the great auricular nerve. All the patients were female and between 50 and 80 years of age.

The author emphasizes the difficulties in attributing the various symptoms in his cases and in those reported in the literature to one and the same local lesion. Not only is there no close regional relationship between the pareses and the skin lesions, but the former may occur before, at the same time as, or up to several weeks after, the skin eruptions. Neither an encephalitis nor a meningitis can explain the symptomatology. The author regards the unilaterality of symptoms as almost the only common feature in the various cases, and that herein lies a clue to their common origin. He suggests that all the symptoms are the result of activation of an unknown virus which affects a pre-existing unilateral *locus minoris resistentiae* in the nervous system. *J. B. Stanton*

SPINAL CORD

530. **Blood-pyruvate Levels in Subacute Combined Degeneration of Cord; Effect of Vitamin B_{12} Therapy**
C. J. Earl, M. F. S. El Hawary, R. H. S. Thompson, and G. R. Webster. *Lancet* [*Lancet*] **1**, 115–116, Jan. 17, 1953. 5 refs.

The authors, working at Guy's Hospital, London, have observed, in 3 previously untreated cases of subacute combined degeneration of the spinal cord, the effect of treatment with vitamin B_{12} on the blood level of pyruvate. When each patient was admitted to hospital the blood content of pyruvate was estimated in the fasting state and at 60 and 90 minutes after a loading dose of glucose had been administered. This was repeated after a course of parenteral treatment with vitamin B_{12}. In all 3 patients the increase in pyruvate level after 90 minutes was significantly greater initially than in controls, but became normal after treatment with vitamin B_{12}.
Walter H. H. Merivale

531. **Lateral Intervertebral Disk Lesions in the Lower Cervical Region**
R. G. Spurling and L. H. Segerberg. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 354–359, Jan. 31, 1953. 6 figs., 9 refs.

The authors, writing from the University of Louisville School of Medicine, Kentucky, give a general review of the diagnosis and treatment of lesions of lower cervical intervertebral disks [no new material is presented]. In discussing the pathological anatomy they point out that almost identical radicular symptoms in the neck and upper extremity may be caused by two different lesions, the first type being the proliferative lesion caused by osteophytic spur formation projecting into the intervertebral foramen, the second type due to acute posterolateral rupture of a cervical disk with direct compression of a nerve root in the intervertebral foramen. Approximately 95% of all cervial lesions occur at the levels of the 5th and 6th disks, those at the 6th being about three times as common as those at the 5th. A history of frank trauma to the neck is obtained in only about one-third of cases; in such cases the onset of radicular symptoms is usually early. The pain in all cases is characteristically increased by coughing and by movements of the neck. Usually the neck is held in a fixed position, and passive movements are resisted. The pain can be reproduced by forcible movement of the head downwards, backwards, or laterally—the neck compression test. Conversely, pain is relieved by manual extension of the head in the line of the spinal axis. Sensory, motor, and reflex changes in the distribution of the roots involved will also be noted. Clinical examination is not wholly reliable. Radiological examination on a tilting table after intrathecal injection of a contrast medium is essential.

The only positive indication for immediate operative treatment is severe neurological deficit due to compression of the spinal cord or weakness and atrophy of muscles of the shoulder girdle or arm. In a series of 110 cases treated by the authors only 33 patients required surgical intervention, 20 of these having failed to respond to conservative treatment and the other 13 having urgent neurological symptoms. The remaining 77 patients were satisfactorily treated by (1) cervical traction intermittently for 7 to 10 days, (2) the administration of 1 g. of mephenesin every 6 hours during the period of traction, and (3) complete rest in bed.
Donald McDonald

532. **Phantom Limb in Paraplegic Patients. Report of Two Cases and an Analysis of its Mechanism**
A. W. Cook and W. H. Druckemiller. *Journal of Neurosurgery* [*J. Neurosurg.*] **9**, 508–516, Sept., 1952. 23 refs.

Two cases are reported from the U.S. Naval Hospital, Long Island, New York, in which the patients, who had suffered complete functional transection of the spinal cord, had the sensation of a phantom limb after amputation of a paraplegic leg. The authors suggest that this finding necessitates the abandonment of theories which postulate that phantom-limb sensation depends on afferent impulses from peripheral nerves in the stump passing to the sensory cortex in the parietal lobe. Instead, they suggest that the memory function of the brain in recalling the body schema is of primary importance and so, in view of the perceptual hallucinations associated with temporal-lobe seizures, the temporal cortex rather than the parietal cortex may be the site of phantom-limb projection. In their view this indicates that, in the management of phantom-limb phenomena, less attention should be paid to local conditions in the stump, as the sensation of a phantom limb may be present when the affected limb is already without sensory connexions.
Donald McDonald

533. **Bodily State in Injuries of the Spinal Cord**
H. Chor, I. Finkelman, and H. Blustein. *Neurology* [*Neurology*] **3**, 111–118, Feb., 1953. 1 fig., 3 refs.

Psychiatry

534. **Electrical Rhythms from the Depth of the Frontal Lobes during Operations on Psychotic Patients**
R. G. BICKFORD, A. UIHLEIN, and M. C. PETERSEN. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **28**, 135–143, March 11, 1953. 4 figs., 6 refs.

Electrical recordings made by means of a probe electrode lowered into the frontal lobe of psychotic patients under local anesthesia indicate the existence of (1) fast rhythms (20 to 30 cycles per second), (2) intermediate frequencies (10 to 15 cycles per second) and (3) slow waves (0·5 to 3 cycles per second). Rhythms 1 and 2 are present in most patients and may be considered as normal rhythms of the frontal lobe. The slow rhythms which were observed in about half of the patients (unilateral in 2) are of interest since they may bear some relationship to an organic disturbance of the frontal lobe in these patients. The results suggest the need for preleukotomy depth recordings as an aid to planning of the leukotomy incision. Leukotomy was found to produce slowing of frequency in the depth recordings. An area of relative electrical inactivity has been located in the depth of the frontal lobe.—[Authors' summary.]

PSYCHOSOMATIC MEDICINE

535. **Psychosomatic Aspects of the Premenstrual Tension Syndrome**
L. REES. *Journal of Mental Science* [*J. ment. Sci.*] **99**, 62–73, Jan., 1953. 1 fig., 29 refs.

The author examined a random sample of 145 women, 61 of whom were normal women and 84 were patients attending psychiatric and allergy clinics in Cardiff and Glamorgan, in respect of menstrual history and symptomatology, family history, childhood neurosis, adjustment to school, work, and marriage, and personality as assessed in terms of general stability and clinical type. In the normal group the Maudsley Medical Questionnaire and Word Connection List were used as ancillary methods of detecting and assessing neurosis. The patients were given charts for recording changes in bodily and mental state observed before the menstrual period. The information collected was then analysed.

It was found that 62% of the patients, compared with 21% of the normal group, had significant premenstrual tension, 32% of the former and only 5% of the latter having severe symptoms. A comparison of women within the normal group with premenstrual tension and those free from it showed no significant difference in incidence of personality instability or neurosis. Thus premenstrual tension may exist in women with little or no evidence of instability, and conversely many women with severe neurosis do not suffer from premenstrual tension. A positive correlation was found between the incidence of " neurotic constitution " (as defined by Slater) and that of premenstrual tension: the greater the predisposition to neurotic breakdown, the greater the intensity of symptoms of premenstrual tension. There was also a positive correlation between the severity of the neurosis and the intensity of premenstrual symptoms.

Many patients with neurosis responded to psychiatric therapy without much improvement in their premenstrual-tension symptoms, while on the other hand it was sometimes possible to relieve these symptoms by means of drugs without affecting the co-existing neurosis. The author believes that bodily changes are the primary factor in this syndrome, but that in unstable or neurotic women the intensity of symptoms and the degree of disability are influenced by psychogenic factors as well.

[This paper is valuable as a field survey of the incidence of premenstrual tension. Its value would be greater if correlations had been worked out between the occurrence of symptoms and the woman's attitude to her female role in sexual activity and childbearing, since it is likely that these attitudes, rather than " neurosis ", determine the intensity of distress.] *Desmond O'Neill*

536. **Tension Headache**
A. P. FRIEDMAN, N. DE SOLA POOL, and T. J. C. VON STORCH. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 174–177, Jan. 17, 1953. 7 refs.

It is the authors' contention that " tension headache " can be differentiated from migraine and conversion (hysterical) and other types of headache. Tension headaches occur only in relation to emotional conflicts, which may be conscious or unconscious, are usually bilateral, frontal or occipital, and possibly associated with evidence of anxiety, as well as with nausea and vomiting. Tension headache cannot be distinguished from conversion headache on the basis of its clinical features only, the distinction of the latter resting on the specific unconscious symbolic meaning of the symptoms, but it can readily be differentiated from migraine on history alone. Of 400 patients with tension headaches seen at the Montefiore Hospital, New York, 69% were females, mostly in the third and fourth decades. In 41% the history went back 10 years or more, and in 23% the headache was constant. In 45% of the patients several different parts of the head were affected, either generally or in succession, and in only 20% was the headache limited to one site.

A large variety of drugs were given, and although it is stated that the most effective symptomatic medication was a combination of analgesic with sedative, it is also admitted that 55% of patients responded to a placebo and 30 to 50% to " almost any medication given them." Psychotherapy with reassurance, suggestion, and re-education was found to be the most effective form of treatment, 58% of patients obtaining substantial relief of their symptoms.

[Many readers will find some difficulty in differentiating this form of psychogenic headache from any other, either on the basis of clinical history, psychogenic factors, or response to any kind of therapy. Stress is laid on the importance of the doctor–patient relationship in treatment, but this is probably true of all human ills.]

Hugh Garland

537. **Emotional Stress in the Precipitation of Congestive Heart Failure**

W. N. CHAMBERS and M. F. REISER. *Psychosomatic Medicine* [*Psychosom. Med.*] **15**, 38–60, Jan–Feb., 1953. 7 figs., 10 refs.

The authors studied 25 patients, admitted consecutively to the Cincinnati General Hospital, with a view to determining the relation between stress and the onset of congestive heart failure. There were 14 men and 11 women, the mean age for both sexes being 58 years. Most of the patients came from the poorest social and economic group; 6 were seen during the initial episode of congestive heart failure, 12 had suffered from chronic failure of varying degree for weeks or years, and 7 had had repeated attacks of acute failure. All had considerable reduction of cardiac reserve, and 5 died within 4 weeks of admission.

Each patient was given, on the average, 3 one-hour interviews by one of the authors. The technique of associative anamnesis was employed and was supplemented where necessary by direct questioning. Regular discussions of the material as it was being gathered were held with the other, the psychiatric observer; members of the patient's family and close associates were also interviewed. The services of social workers were utilized. From these studies of the patient and his environment an attempt was made to determine his situation at the time of the onset of the failure.

Precipitating factors could be identified in 23 of the 25 patients. In 19 it was felt that emotional tension was the factor immediately responsible for increasing the work load of the heart beyond its capacity; in 4 patients organic factors such as pulmonary infarction were held to be responsible; in the other 2 it was impossible to isolate a single precipitating factor. Emotional tension at the material times can be grouped under two headings: (1) events leading to feelings of rejection and loss of security; and (2) events leading to feelings of frustration and rage. Thus some situation to which the patient reacted strongly proved very often to have acted as " the straw that broke the camel's back ".

Desmond O'Neill

538. **Rejection Dyspepsia**

G. G. ROBERTSON. *Lancet* [*Lancet*] **1**, 63–66, Jan. 10, 1953. 3 refs.

It is suggested that the syndrome of abdominal distension, eructation of wind and of small quantities of gastric secretion, nausea, and occasional vomiting in women, may be a physical manifestation of their rejection of coitus. Clinical observations in a large number of cases seen in private practice showed that attacks of dyspepsia were associated with sexual experiences which were unpleasant to the patient. The syndrome is, as might be expected, rare in the male. Of 300 patients with severe flatulent dyspepsia, only one was male, and only 3 were single women. Of the rest, 162 had been frigid throughout marriage and 128 had become frigid after marriage; of the former group 83% had an unduly strong mother-attachment.

[This paper is important because it reminds the clinician that the origins of some forms of dyspepsia are to be sought not in the physical but in the emotional field. However, not everyone will agree with the author's estimation of the importance of frigidity as a determinant; it may be, for example, that rejection of the female role as a whole is the primary condition.]

Desmond O'Neill

539. **Raynaud's Disease. Psychogenic Factors and Psychotherapy**

J. A. P. MILLET, H. LIEF, and B. MITTELMANN. *Psychosomatic Medicine* [*Psychosom. Med.*] **15**, 61–65, Jan–Feb., 1953. 17 refs.

The authors, writing from the Columbia–Presbyterian Medical Center, New York, cite the case records of 4 patients with Raynaud's disease in support of the hypothesis that emotional tension has an important role in this disorder.

According to them, the first attack of Raynaud's disease generally appears to follow an emotionally charged experience, subsequent attacks being often provoked by emotional tension. The most striking examples of such attacks are those which occur at interviews when an acute emotional state is aroused. The dominant element in the emotional background of Raynaud's disease seems to be a feeling of guilt and fear of retribution; in the authors' cases, the main source of guilt was self-blame for the death of some member of the immediate family. After a course of analytical psychotherapy 2 patients have remained well for over a year and 2 have responded well but are still under treatment.

Desmond O'Neill

TREATMENT IN PSYCHIATRY

540. **A Comparison between Unidirectional Current Nonconvulsive Electrical Stimulation Given with Reiter's Machine, Standard Alternating Current Electroshock (Cerletti Method), and Pentothal in Chronic Schizophrenia**

D. H. MILLER, J. CLANCY, and E. CUMMING. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **109**, 617–620, Feb., 1953. 9 refs.

At the Saskatchewan Hospital, Weyburn, Saskatchewan, 30 patients originally diagnosed as suffering from catatonic schizophrenia, none of whom had received any treatment during the preceding year, were divided into 3 groups of 10, one being given electric convulsion therapy (E.C.T.), one treated by rapid anaesthetization with thiopentone, and one by non-convulsive electric stimulation for 5 minutes with Reiter's machine set at high modulation and a current of 5 mA, the patient being anaesthetized with thiopentone. E.C.T. was given 5

times weekly for 3 weeks, and the other treatments were given 5 times weekly for 4 weeks. The environmental conditions provided wide opportunities for the patient to engage in active occupations. Two of the authors and, independently, two other physicians assessed the state of psychosis, while ward behaviour was assessed by at least 4 members of the ward staff.

Application of the χ^2 test [the manner of its application is not described, and its validity appears questionable] in the comparison of results based on a number of different factors showed very few significant differences between the groups after treatment, although the patients as a whole showed a significant degree of improvement in respect of activity and interest in their environment, while 3 patients who had been incontinent of faeces became continent, 2 after non-convulsive stimulation and one after thiopentone treatment. The number of patients " demonstrably hallucinating " rose during treatment from 20 to 30, this being interpreted as a defence mechanism against greater participation in a real world; otherwise, there was no significant change in the psychotic picture. *N. A. Standen*

541. **Use of Succinylcholine in E.C.T., with Particular Reference to its Effect on Blood Pressure**
D. J. ADDERLEY and M. HAMILTON. *British Medical Journal* [*Brit. med. J.*] **1**, 195–197, Jan. 24, 1953. 5 refs.

The authors investigated changes in blood pressure occurring during electric convulsion therapy (E.C.T.) when a short-acting muscle relaxant—succinylcholine (" scoline ")—was used. Their subjects were all women, mostly elderly, feeble, and hypertensive.

The results observed were: (1) the preliminary injection of 0·2 g. of sodium thiopentone, necessary to produce unconsciousness, caused a fall in both systolic and diastolic blood pressure. (2) The injection of 1·5 ml. of a 5% solution of succinylcholine raised the blood pressure to a level higher than the original one, the difference being statistically significant. The injection of sterile water in place of the relaxant had no effect on the blood pressure. (3) The electric convulsion, administered after a few breaths of oxygen containing 5% carbon dioxide, caused no further change in blood pressure. (4) The rise in blood pressure after succinylcholine could be prevented by the injection of a ganglion-blocking agent, such as tetraethylammonium bromide or hexamethonium iodide (" hexathide ").

The authors also give an account of their routine technique when using succinylcholine in E.C.T. They mention two methods of determining whether an adequate convulsive dose of electric current has been applied to a completely relaxed patient. In the first method dilatation of the pupils and injection of the conjunctivae are used as the criteria, but when ganglion-blocking agents have been used this method may be deceptive. They then adopt the second method, in which arterial compression is applied to one arm before the injection of succinylcholine into the other. The compression is then maintained while the current is applied, when a slightly modified clonic fit in the blocked arm can be observed. *F. K. Taylor*

542. **Electronarcosis and Prolonged Electric Shock in Psychiatric Treatment.** (L'électronarcose et l'électrochoc prolongé en thérapeutique psychiatrique)
V. J. DURAND. *Annales médico-psychologiques* [*Ann. méd.-psychol.*] **111**, 19–71, Jan., 1953. Bibliography

The history of electric convulsion therapy (E.C.T.) is reviewed and various recent modifications are described. In particular, the technique and clinical, physiological, and psychological effects of electronarcosis and prolonged electric shock are compared with each other and with those of the ordinary forms of E.C.T. Indications, complications, and hypotheses concerning the mechanism of action are discussed. Observations made on 84 female patients treated with prolonged electric shock at the Saint-Venan Mental Hospital are recorded and the results compared with others reported in the literature, with which they show general agreement. (The number of patients treated by electronarcosis was small and these are not included in the series.)

The technique of prolonged electric shock therapy was that described by Lapipe and Rondepierre at the Besançon Congress in 1950, in which the unpremedicated patient receives a brief initial shock of sufficient intensity to induce immediate unconsciousness, after which a current of about 150 mA is maintained for 50 to 60 seconds. The frequency and total number of sessions varied according to the nature of the disease and the response to treatment; thus, depressives were given treatment every other day, whereas those in whom excitement or confusion predominated were treated as often as 4 times daily for the first week. The results were as follows:

Diagnosis	No. of Patients Treated	Cured	Much Improved	Slightly or Transiently Improved	Not Improved
Depressive states	30	9	15	6	0
Manic states ..	7	3	3	1	0
Schizophrenia and dementia praecox ..	25	2	6	14	3
Confusional and puerperal psychoses and acute agitated excitement states ..	7	2	5	0	0
Chronic agitated excitement states ..	7	0	1	5	1
Psychoneuroses	5	2	1	2	0
Miscellaneous psychoses ..	3	0	2	1	0
Total	84	18	33	29	4

It is claimed that these results and those reported in the literature, taken in conjunction with the relative simplicity, safety, and freedom from serious complications of the method, warrant the more extensive use of prolonged electric shock in the treatment of mental disorders. Examples are also cited from the literature to stress the value of electronarcosis, the clinical indications being very similar to those for prolonged electric shock. *Adrian V. Adams*

Dermatology

543. **Hair Loss from Sebum**
P. FLESCH. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **67**, 1–9,. Jan. 1953. 6 figs. 36 refs.

In experiments carried out at the University of Pennsylvania the author found that the application of sebum, extracted from human hair with ether, to the skin of animals caused inflammation, keratinization, and temporary loss of hair in all rabbits tested and in 10 out of 23 mice, though no hair loss occurred in guinea-pigs. Both the saponifiable and unsaponifiable fractions of sebum had the same effect on rabbits' skin, and oleic and linoleic acids, two of the unsaturated components of sebum, were also shown to be potent depilatory agents in all species tested. Squalene, another unsaturated component, has already been shown to have a depilatory action on animals' skin (Flesch, *Proc. Soc. exp. Biol.* (*N.Y.*), 1951, **76**, 801) though no such action has yet been demonstrated experimentally on human skin. The depilatory effect of sebum and its components (which is thought to be due to inactivation of free sulphydryl groups and the sulphydryl enzyme, succinic dehyrogenase) is discussed in relation to hair growth and keratinization and the natural hair cycle in man and animals. *John T. Ingram*

544. **Use of Dimercaprol (BAL) Ointment in Chronic Chrome Dermatitis**
H. N. COLE. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **67**, 30–36, Jan., 1953. 5 figs., 8 refs.

In an investigation at the Western Reserve University and Hospital, Cleveland, Ohio, zinc oxide paste with 3% dimercaprol was found to relieve experimentally produced chrome dermatitis in rabbits. The same treatment also led to improvement in 6 of 7 patients suffering from chrome dermatitis; the condition of the 7th patient was, however, aggravated by the dimercaprol.
John T. Ingram

545. **Studies of Skin Hypersensitivity to Lanolin**
M. B. SULZBERGER, T. WARSHAW, and F. HERRMANN. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **20**, 33–43, Jan., 1953. 8 refs.

In view of the widespread use of lanolin in ointments, cosmetics, and other products in daily use, the authors have made a further attempt to discover the fraction or constituent responsible for occasional allergic reactions, and its relationship to the constituents of human sebum. At New York University Hospital patch tests with anhydrous lanolin were carried out on 1,048 patients with various dermatological ailments and 120 healthy controls, those giving a positive reaction (12 of the 1,048 patients; none of the controls) being subjected to further patch tests with various lanolin derivatives. The methods used, the constituents and fractions employed, and the results obtained are described and discussed. The results confirm previous findings that the active allergenic material resides in the fraction containing the aliphatic alcohols. *G. B. Mitchell-Heggs*

546. **Benign Familial Pemphigus. Cytology and Nosology**
L. H. WINER and A. J. LEEB. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **67**, 77–83, Jan., 1953. 3 figs., 13 refs.

The authors studied the histology and cytology of "benign familial pemphigus" in 5 patients at the Wadsworth General Hospital, Los Angeles. They state that lysis of the epidermis with intra-epidermal vesicle formation is consistently found in this disease. Examination of smears obtained from the vesicle by the Tzanck technique showed great numbers of lysed epithelial cells of oval or rounded outline as well as normal epidermal cells. These lysed cells have large vesicular nuclei with one or more large, distinct nucleoli situated in the centre of the nucleus. The nuclear chromatin is reticulated, and the cytoplasm stains a bright lavender colour with Giemsa and is finely granular. In 2 of the 5 cases examined eosinophilic granular masses very suggestive of "grain cells" were present, and adjacent to these were doubly refractile cells resembling *corps ronds*.

The authors conclude that benign familial pemphigus is badly named, as in their view it is a delayed epidermal naevus and should be regarded as bullous keratosis follicularis (Darier's disease). *H. R. Vickers*

547. **Clinical and Histological Criteria of Lichen Planus of Skin and Mucosa.** (Critères cliniques et histologiques des lichens plans cutanés et muqueux; délimitation)
H. GOUGEROT and A. CIVATTE. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph.* (*Paris*)] **80**, 5–29, Jan.–Feb., 1953. 15 figs.

From the Hôpital Saint-Louis, Paris, the authors discuss the results of their study of lichen planus, with particular reference to atypical forms. They divide their paper into two parts, of which the first, by Gougerot, deals with the clinical criteria, and the second, by Civatte, with the histological criteria.

Gougerot describes the following forms: (1) erythemato-squamous plaques which may precede a typical lichen planus; (2) erythematous and erythemato-squamous lesions, associated with the classical papules, which may resemble parakeratosis, pityriasis rosea, or even an atypical psoriasis; and (3) pigmenting lichen. This last form may be related to what the author calls "invisible" lichen planus, in that pigmentation may follow pruritus due to a lichen planus that has produced no intermediate lesions. Other invisible lichens (pruri-

tus) may precede, sometimes by years, the typical or atypical eruption, or may remain after the eruption disappears. [The concept of " invisible lichen " which is never associated with visible lesions but is cured by arsenic or other remedies appropriate to lichen planus seems to be somewhat far-fetched.] Atypical forms of lichen on the buccal mucosa are: (1) sclero-atrophic or sclerous lichen occurring in bands on the tongue, resembling syphilitic glossitis; (2) punctate papillary forms or lichen planus of the tips of the lingual papillae; (3) pavemented lichen planus; (4) xerostomic lichen planus; (5) erosive forms, associated particularly with gold intoxication; (6) invisible eruptions; pruritus or paraesthesiae associated with lesions elsewhere or preceding or persisting after lesions in the mouth. The author gives his arguments in favour of relating lichen sclerosus (also called lichen albus or *porcelainé*) to lichen planus. In the second part of the paper Civatte surveys and illustrates the histological appearances in the typical lichen papule, and describes the stages in its development, as well as the appearances in the buccal mucosa and also in the atypical forms, lichen planus corneus, circinate atrophic lichen planus, bullous lichen planus, and lichen nitidus. Histologically, lichen sclerosus seems to bear no resemblance to lichen planus. The difficulties in differential diagnosis between lichen planus, subacute lupus erythematosus, and pigmented reticulate poikilodermia are discussed.

[This excellent paper should be studied in the original.]

James Marshall

548. **Malignant Melanoma. A Clinicopathological Analysis of the Criteria for Diagnosis and Prognosis**

A. C. ALLEN and S. SPITZ. *Cancer* [*Cancer (N.Y.)*] **6**, 1–45, Jan., 1953. 59 figs., 27 refs.

This exhaustive survey is based on the study of 934 cases of malignant melanoma treated at the Memorial Center, New York; in 337 of these cases histological sections of the primary lesions were available and an adequate follow-up had been carried out over a period of at least 5 years, and this group therefore forms the main source of the authors' material. They classify pigmented naevi as follows:

(A) BENIGN. (1) Intradermal naevi (common moles), which may be smooth, papillary, or hairy, and of various shades of brown; they are exceedingly rare on the soles, palms, and genitalia, and they do not undergo malignant change. (2) Junctional naevi, which tend to be hairless, smooth, and flat or only slightly raised, and are of various shades of brown; they are located entirely within the epidermis and may occur in the skin of any part of the body and in the mucous membranes of certain regions. Pigmented blemishes on the genitalia, the soles, the palms, and the digits " should be considered wholly, or at least in part, junctional ". While only a small proportion of junctional naevi become malignant, it is the authors' opinion that every melanocarcinoma of the skin or mucous membranes, with the exception of the rare malignant blue naevus, arises from a junctional or compound naevus. (3) Compound, composed of an intradermal and an immediately overlying junctional naevus. The compound naevus may undergo transformation into a melanocarcinoma by virtue of its junctional component. (4) Juvenile melanomata, the histological picture of which may closely simulate, or may be indistinguishable from, that of the adult melanocarcinoma, though in about two-thirds of the cases it is possible to differentiate the two conditions. (5) Blue naevi (Jadassohn–Tièche). These occur predominantly on the buttocks and the dorsum of the feet and hands, though they may be found also on other parts of the body, particularly the face. They are usually smooth, brown to blue-black in colour, and hairless. Malignant transformation of these naevi is rare.

(B) MALIGNANT. (1) Melanocarcinomata may be superficial or deep, the latter having a far worse prognosis than the former. (2) Malignant blue naevi.

Amongst the many clinical observations recorded, the following may be of general interest. Melanocarcinoma of the mucous membranes (urogenital, anorectal, head and neck regions) has an almost uniformly fatal outcome. In a patient with a melanocarcinoma activation of junctional naevi may occur in any part of the body, but particularly in the vicinity of the primary tumour. A relatively high proportion (68·3%) of the patients in this series who survived 5 years or longer were treated merely by local excision of the primary tumour. The prognosis of cutaneous melanocarcinoma is better in women than in men; this is especially true for tumours of the head and neck region. A patient with a small primary melanocarcinoma, especially one that is not ulcerated, has an appreciably better prognosis than a patient with a large ulcerated lesion.

[This important paper is beautifully illustrated by photomicrographs.] *N. Alders*

549. **Effects of the Resin of Euphorbium on Verrucae Plantares—Human and Animal Experimentation**

R. W. GOLDBLUM and A. C. CURTIS. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **20**, 45–50, Jan., 1953. 2 figs., 5 refs.

The effect on verrucae plantares of euphorbium, the resin of *Euphorbia resinifera*, which has been used as a household remedy for warts for many years, was studied in 60 cases at the University of Michigan Hospital, Ann Arbor. The patients' ages ranged from 7 to 78 years, and the number of warts from 1 to 7. The wart was pared and a 30% solution of euphorbium in 95% alcohol applied to the central keratotic area and covered with adhesive tape. This process was repeated at 48-hour intervals, it being usually possible to remove the verruca entirely after 2 or 3 treatments. Only in 2 cases did the wart return during a 4-month observation period. The histological appearance of normal human and animal skin treated with the resin is described.

(During the discussion of this paper other instances of popular household remedies for warts whose effects have been confirmed on scientific study were mentioned. It was felt that although the results of the present trial were impressive, it was essential in this disease to have control-treated material for comparison.)

G. B. Mitchell-Heggs

The Breast

550. Cancer of the Breast and the Menopause
D. W. SMITHERS. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol.*] **4**, 89–95, Oct., 1952. 5 figs., 5 refs.

In order to stimulate further thought on endocrine control of carcinoma of the breast, the author, writing from the Royal Cancer Hospital, London, reviews the historical steps which have led to the present position of treatment. He adduces statistical evidence that the incidence and prognosis of carcinoma of the breast are affected by the menopause, and describes 3 personal cases, occurring in nulliparous women, of marked, though temporary, regression of the tumour during the menopause. He points out that assessment of the results of endocrine therapy is difficult and that it is necessary to discount the sense of well-being and the improvement in general health produced by testosterone. Radiological changes in the skeleton may be produced not only by metastases but also by post-menopausal osteoporosis and even, in some cases, by secondary deposits of tumour in the endocrine glands leading indirectly to skeletal changes. It is probable that objective signs of response to hormone therapy are seen in only 20% or less of the patients treated. The author suggests that an improvement in this respect is not likely until a more accurate conception of the relation of the tumour cell to its hormonal environment is arrived at.

E. Stanley Lee

551. Relationship between Benign Breast Disease and Cancer
E. F. LEWISON and J. G. LYONS. *Archives of Surgery* [*Arch. Surg.* (*Chicago*)] **66**, 94–114, Jan., 1953. 2 figs., 36 refs.

This paper begins with a very full historical review of breast disease, starting with the Edwin Smith papyrus (1600 B.C.), referring in passing to the observations on breast disease of Ambroise Paré, John Hunter, Sir Astley Cooper, and others, and finally paying tribute to the work of Cheatle and Cutler. The authors then describe the results of a follow-up investigation of cases of benign breast disease treated surgically at the Johns Hopkins Hospital, Baltimore, during the period 1925–41 inclusive.

Out of a total of 451 patients treated, 385 were traced, there being 200 cases of fibroadenoma, 153 of fibroadenosis, and 32 of papilloma. In 33 cases (8·7%) the patient had been subjected to mastectomy, so that the chances of developing carcinoma subsequently must be regarded as diminished in this group as compared with the remainder. Benign disease recurred in 50 patients (13%), and 7 patients (1·8%) developed cancer of the breast. In 4 of the 7 the cancer developed on the side opposite from that of the original benign disease.

The authors then consider whether this incidence of cancer indicates a predisposition of patients with benign breast disease to develop malignant disease. Since the average period of follow-up in their cases was 13·6 years and the average age when treated was 36 years, they calculate the expected incidence in a comparable section of the whole population of the United States by averaging the mortality rates from cancer of the breast for the age range 35 to 50 years (as given in official tables for 1946) to give an annual mortality rate of 0·052%, which in 13·6 years would give a mortality of 0·7%. This figure [which is taken to represent the expected incidence of the disease] is 2·6 times less than the observed rate of 1·8%, a factor rather less than that of 4·5 reported by Warren (*Surg. Gynec. Obstet.*, 1940, **71**, 257).

This statistical evidence is supported by the findings in the experimental laboratory, where the administration of oestrogens can be shown to produce benign breast disease in animals and, in fuller doses, carcinoma. Moreover, every stage between normal and carcinomatous breast tissue, passing through the various phases of fibroadenosis on the way, can be demonstrated histologically. The authors, however, would place little reliance on this experimental and histological evidence. They stress the dangers of drawing conclusions in regard to human pathology from the results of experiments performed on animals, and point out that it is quite impossible to produce fibroadenosis followed by cancer in primates by the injection of oestrogens, in whatever doses these are administered. Furthermore, the compilation of so-called series of histological sections showing an apparently progressive process of change in no way proves conclusively that the same changes occur in any one case [and does not dispose of the possibility that cancer may be grafted on to any of these stages with equal facility]. Nevertheless, as they state, there is a hard core of reliable statistical evidence that the tendency to cancerous change in women suffering from benign breast disease is greater than in normal women of the same age. Fortunately this increased tendency is not great enough to warrant any action other than a periodic examination of the breasts and indeed, bearing in mind the authors' findings that in 4 out of 7 cases the cancer developed in the contralateral breast, the only logical preventive treatment in such cases would be to remove both breasts [which is, of course, unthinkable in so common a disease].

[This paper gives a most judicious appraisal of the position in regard to benign breast disease, and although perhaps no new facts emerge, those facts which are already known are presented in a clear and scientifically acceptable manner.] *H. J. B. Atkins*

552. Cystosarcoma Phyllodes of the Breast
H. E. STEPHENSON, S. GROSS, S. L. GUMPORT, and H. W. MEYER. *Annals of Surgery* [*Ann. Surg.*] **136**, 856–863, Nov., 1952. Bibliography

Paediatrics

553. **Renal Water Excretion in Premature Infants**
H. L. BARNETT, J. VESTERDAL, H. MCNAMARA, and H. D. LAUSON. *Journal of Clinical Investigation* [*J. clin. Invest.*] **31**, 1069–1073, Dec., 1952. 4 figs., 18 refs.

This paper from the New York Hospital—Cornell Medical Center gives an account of an investigation undertaken to test the generally accepted statement that the young infant cannot respond to an increase in fluid intake by passing either more urine or a more dilute urine. The renal response of 4 premature infants aged 5 to 8 days and weighing between 1·84 and 2·21 kg. and of one premature infant weighing 2·46 kg. (at 36 days) was compared with that of 2 adults and one infant of 18 months. The following measurements were made: (1) glomerular filtration rate, (2) concentration of osmotically active urinary solutes, (3) rate of excretion of urinary solutes. The infants were given an artificial-milk diet and were kept in an air-conditioned metabolism unit.

It was found that none of these infants was limited in its ability to increase urinary output when given more than the usual amount of fluid. Various possibilities are discussed to account for the difference between this finding and those of other workers—one which is worth noting being that the latter were affected by the infant's response to painful stimuli such as venepuncture, which in one case cited interrupted diuresis for one hour.

While the results here reported do not necessarily demonstrate that the premature infant in the immediate postnatal period responds to a high fluid intake as well as older infants and adults, the fact that this was the case in infants 5 to 8 days old suggests at least a very rapid development of postnatal renal function. It is calculated from the above observations that the young premature infant can excrete as much as 20 ml. of water per mOs. of solute; the authors point out that this value, which constitutes a definition of maximum renal water excretion, is the same for infants as for adults.

A. T. Macqueen

INFANT FEEDING

554. **Renal Water Requirement of Infants Fed Evaporated Milk with and without Added Carbohydrate**
E. L. PRATT and S. E. SNYDERMAN. *Pediatrics* [*Pediatrics*] **11**, 65–69, Jan., 1953. 2 figs., 11 refs.

In an investigation carried out at Bellevue Hospital, New York, the authors studied the effect on the renal water requirement of 6 male premature babies aged 10 to 30 days of giving their feeds of diluted evaporated milk with and without added carbohydrate, the aim being to estimate the danger of causing dehydration. The feed consisted either of 100 ml. of evaporated cow's milk with 14·2 g. of " dextrimaltose " to which water was added to make a volume of 220 ml., or of 100 ml. of the evaporated milk diluted to a volume of 155 ml., the caloric value in either case being 0·9 Calorie per ml., and each baby was given sufficient to supply a fixed number of calories. The babies were fed for 3 days on each feed and on the second and third days a 24-hour specimen of urine was collected and the volume measured. The solute content was estimated by calculating the depression of the freezing point, using a cryoscope fitted with a Beckman thermometer.

The concentrated unsweetened feed contained so much more (about 40%) protein and minerals that the urinary solute load was increased by 85%. The varying quantity of water necessary to excrete this added load at various urinary concentrations is shown in a graph. The authors conclude that the feeds, if given at the usual concentration of 20 Calories per oz. (0·7 Cal. per ml.), would in either case supply adequate water for the excretion of their renal residue. If given in a more concentrated form, or if extrarenal water loss were high, the concentrated unsweetened feed would then require a quantity of renal water which might compromise the water balance and well-being of the child.

H. G. Farquhar

555. **Breast-feeding in the Oxford Child Health Survey. Part I. A Study of Maternal Factors**
C. WESTROPP. *British Medical Journal* [*Brit. med. J.*] **1**, 138–140, Jan. 17, 1953. 26 refs.

The relation of certain maternal factors to success or failure in breast-feeding among 574 mothers included in the Oxford Child Health Survey was studied at the Institute of Social Medicine, Oxford. Three groups of mothers were distinguished: (1) those who breast-fed their babies for 4 months or more (53·8%); (2) those who breast-fed for more than 3 weeks but less than 4 months (30%); and (3) those in whom lactation was never firmly established (16·2%). The factors considered were age and parity, physique and health, social and economic circumstances, maternal efficiency, and mode, place, and time of delivery. As previous workers have found, age appeared to play no significant part in determining the duration of breast-feeding. Previous experience of maternity, however, had a significant effect which differed in different social classes, the incidence of prolonged breast-feeding increasing steadily with increasing size of family in Classes I and II, whereas in all other classes the incidence was higher among mothers with 2 or 3 children than among those with one and those with 4 or more. Physique bore no relation to breast-feeding habits, but there was a marked difference in respect of lactation between mothers with " good health " and those with " poor health " after delivery. [No mention is made of the criteria used in determining these.] In assessing the social and economic circumstances an " amenities rating " was applied, as giving a more

reliable index of material prosperity than the Registrar General's occupational classification, the rating being based on such factors as garden facilities, household density, paid helpers, and sanitary facilities; although no significant correlation could be shown between duration of breast-feeding and any of the individual components of the amenities rating, a significant cumulative effect was demonstrable. Maternal efficiency was assessed after three home visits on the basis of a number of subjective factors; a close correlation was found between successful breast-feeding and maternal efficiency, but the interpretation of this finding is difficult, since maternal efficiency is also correlated with social class, health, and parity. Less than half the babies were born at home, and the proportion of these which were successfully breast-fed was the same in all social classes; this was in contrast to the findings for babies born in institutions, successful breast-feeding being considerably less frequent in this group among mothers in Classes IV and V (who, however, included an exceptionally large proportion of cases of ill health or obstetrical emergency).

The author emphasizes that much still remains to be learned about breast-feeding and the factors that influence it, of which the social and economic, forming what Ryle called " the complex of adverse circumstances which accompany poverty ", play no small part. But although this is confirmed by the results of the present survey, little progress has yet been made in determining which of the individual factors is responsible for the most harm.

David Morris

556. **Management of Breast Feeding**

G. R. Barnes, A. N. Lethin, E. B. Jackson, and N. Shea. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **151**, 192–199, Jan. 17, 1953. 2 figs., 11 refs.

The authors describe in detail the management of breast-feeding at the Grace–New Haven Hospital, Connecticut. As they point out [rightly] " much that is described is not new . . . often, however, it is the regard for small items that makes the difference between success and failure for the nursing mother ". In prenatal preparation for breast-feeding manual expression is not taught as a routine; " plucking " is still advised for retracted nipples [but scant mention is made of the use of glass shields, and the importance of a well-fitting brassiere is emphasized only in the discussion on postnatal care.] Glucose water is advised for complementary feeding for the infant during the first week [this is not now a frequent practice in Britain].

One of the authors has classified infants according to their feeding characteristics as " barracudas ", excited ineffectives, procrastinators, gourmets, and resters. These feeding characteristics are described in detail, but it is pointed out that many infants do not fall into any of these categories. " Frequency days " (generally between the 3rd and 6th days), when infants on a self-demand schedule take feeds oftener than they do before or after this period, are well described. The authors make a clinical distinction between " areolar " engorgement and peripheral engorgement; the former is confined to the areolar area and is treated by ensuring wherever possible that the baby gets the breast well into the mouth: the latter, which involves the whole breast, is treated by administration of codeine, by application of ice bags or warm packs, by the use of binders to lift the breasts, and by manual expression.

Although the authors have had little experience of the administration of stilboestrol [which is often given in Britain] they point out the danger of over-dosage, when the mother may lose her milk. For cracked nipples they advise resting the breast from feeding and manual expression, with local application of balsam of Peru. Since the lying-in period at the Grace–New Haven Hospital is usually less than a week many of these problems and difficulties do not arise until the mother is at home again; this is considered to be responsible for many failures to breast-feed. It is emphasized that a sympathetic and helpful attitude on the part of nurses, obstetricians, and paediatricians is necessary if mothers are to breast-feed their infants successfully.

[Apart from such procedures as " flexible " or " demand " feeding and " rooming-in ", there is much similarity of practice between maternity hospitals in Britain and the U.S.A. Excellent line drawings are reproduced, demonstrating the way in which the infant obtains milk from the breast and the common mistakes in feeding technique.] *David Morris*

CLINICAL PAEDIATRICS

557. **Skeletal Maturational Progress of Children with Chronic Nutritive Failure. Effect of Dietary Supplement of Reconstituted Milk Solids**

T. D. Spies, S. Dreizen, R. M. Snodgrasse, G. S. Parker, and C. Currie. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **85**, 1–12, Jan., 1953. 5 figs., 5 refs.

The authors, at the Jefferson–Hillman Hospital, Birmingham, Alabama, studied the effect on growth of a dietary supplement of reconstituted milk solids in children with chronic nutritive failure and retarded growth. For this purpose some 200 children were subjected to clinical, dietetic, haematological, and radiological examination, and as a result 82 were selected as being suitable for the investigation. These children were paired according to sex, physique, growth, state of health, and socio-economic background, one of the pair being given the supplement and the other acting as a control.

Of the 41 children in the treated group, 19 received a whole-milk and 22 a skimmed-milk supplement of 3 [U.S.] quarts (2·8 litres) weekly for 40 months, and their progress was followed by complete examination as described above, first at 4-monthly intervals and later at 2-monthly intervals. After 40 months the 19 children in the first group were given a weekly supplement of 12 quarts (11·3 litres) of whole or skimmed milk, the remaining 22 continuing as before on 3 quarts weekly. At the start of the investigation the skeletal age of all the children was less than their chronological age.

Children receiving a supplement of 3 quarts of whole or skimmed milk showed little improvement in bone maturation during the first 40 months as compared with the controls, but during the next 6 months improvement was greater. The children given the 12-quart supplement showed a marked increase in the rate of maturation (up to 93%) as compared with the controls; those receiving the 3-quart supplement showed a proportionately smaller increase.

The authors state that the addition of 3 quarts of milk weekly to the children's diet failed to bring their total intake of calories, calcium, iron, vitamin A, aneurin, and ascorbic acid up to the requirements of the Council on Foods and Nutrition of the National Research Council; the 12-quart supplement, while satisfying the recommended requirements of calories, protein, calcium, vitamin A, aneurin, and riboflavin, still left the diet inadequate in iron, ascorbic acid, and nicotinic acid.

H. A. Magee

558. **Glycogen Disease in Infancy in the Form of a Cerebrospinal Disease with Fatal Outcome.** (Die Glykogenose des Säuglings unter dem Bilde einer tödlich verlaufenden cerebrospinalen Erkrankung)
W. SELBERG. *Zeitschrift für Kinderheilkunde* [*Z. Kinderheilk.*] **72**, 306–320, 1952. 7 figs., 12 refs.

The author reports, from St. George's Hospital, Hamburg, 2 cases of a glycogen-storage disease affecting a brother and a sister born in 1947 and 1949 respectively. Both died during the first year of infancy showing signs and symptoms of ascending paralysis. The glycogen deposits were found mainly in the skeletal muscles and the motor tracts of the central nervous system, the specific elements of which showed very severe degenerative changes.

Similar cases have so far been described in only three families. The disease is congenital, clinically very closely resembles Werdnig–Hoffmann's amyotonia congenita, and terminates fatally. In the 2 cases described there was no evidence of the blood incompatibility which some authors have suspected of being present in families in which glycogen disease occurs. *W. Mestitz*

559. **Acute Benign Pericarditis. A Report of Four Cases in Childhood**
B. D. BOWER and J. GERRARD. *British Medical Journal* [*Brit. med. J.*] **1**, 244–247, Jan. 31, 1953. 4 figs., 10 refs.

Acute benign pericarditis occurs in children and is remarkable in that it is not rheumatic, tuberculous, or pyogenic in aetiology, and that it is not amenable to any known treatment, apart from aspiration if the effusion is large. The course of the disease is short and sharp and appears to be self-limiting. It is of remarkable intensity at first, terminating abruptly with complete resolution and without complications or after-effects. A brief description is given, illustrated by radiographs, of 4 cases treated at the Birmingham Children's Hospital, between 1942 and 1951, 2 of which were diagnosed only in retrospect.

Although no evidence has been found of infection with the Coxsackie or other viruses in cases of this disease, which is much better known in the U.S.A. than in Europe, certain features suggest that it may be a manifestation or a complication of Bornholm disease. [It would be well if this malady were kept in mind, especially by those working among children and young people and, if suspected, virus neutralization tests performed which might assist in elucidating its cause.] *G. F. Walker*

560. **On the Natural Regression of Pulmonary Cysts during Early Infancy**
J. CAFFEY. *Pediatrics* [*Pediatrics*] **11**, 48–64, Jan., 1953. 9 figs., 21 refs.

The author describes in detail (with radiographs) 8 cases of pulmonary cyst and 2 cases of pyopneumothorax in infants under 6 months of age which had been under his care in the Department of Paediatrics, Columbia University, and the Babies Hospital, New York. He refers in less detail to 3 other cases of pyopneumothorax and obstructive emphysema. All the 12 of these cases which could be traced became radiologically normal without surgical interference.

The author discusses the aetiology of these cysts and the difficulty of deciding from the radiological picture whether the cysts are in the lung tissue, in the pleural cavity, or involving both owing to leakage from the lung tissue into the pleural cavity. In view of the extreme rarity of these cysts in the foetus and in the immediate neonatal period he doubts their congenital origin. Previous evidence in favour of such congenital origin is discussed and criticized.

In view of the uniformly good prognosis the author advises that surgical interference should not in the first place be considered for these lesions save in the rare case in which a cyst increases in size so rapidly that there is danger of respiratory obstruction. *H. G. Farquhar*

561. **Infantile Eczema and Self-regulated Feeding.** (Eczema ed autoalimentazione del lattante)
F. COPELLO. *Lattante* [*Lattante*] **23**, 895–900, Dec., 1952. 1 fig.

In his work in the Paediatric Department of the Giannina Gaslini Institute, Genoa, the author has observed that in certain babies infantile eczema is associated with difficulty in establishing breast-feeding. Of 47 infants with eczema, 21 showed no such signs of intolerance and were kept at the breast. In these cases the condition cleared up in an average time of 7 weeks and there were few relapses; these infants were in general large and placid. The remaining 26 however were small, active babies, who did not take quickly to breast-feeding. Of these, 14 were kept at the breast, but their times of feeding were freely self-regulated. In these cases the eczema responded more slowly and there were more relapses than in either the first group or in a third (control) group of 12 infants who were given a prepared acidified milk mixture.

The author believes that a study of the individual infant's reaction to breast-feeding is important and, where intolerance occurs, a change to suitable artificial feeding is more beneficial than self-demand feeding.

A. Paton

Public Health and Industrial Medicine

562. **An Epidemic of Influenza due to Virus B**
T. ANDERSON, N. R. GRIST, J. B. LANDSMAN, S. I. A. LAIDLAW, and I. B. L. WEIR. *British Medical Journal* [*Brit. med. J.*] **1**, 7–11, Jan. 3, 1953. 2 figs., 1 ref.

The authors describe an epidemic of influenza due to Type-B virus which occurred in Glasgow in the early months of 1952. The epidemic was a large one confined to a period of approximately 5 weeks. When this outbreak was compared with a previous epidemic of similar size due to Type-A virus it was found that although the incidence of pneumonia in the two epidemics was very similar, the mortality from pneumonia in the Type-A epidemic was slightly higher. *R. S. Illingworth*

563. **Tuberculosis and Social Conditions in the Metropolitan Boroughs of London**
B. BENJAMIN. *British Journal of Tuberculosis* [*Brit. J. Tuberc.*] **47**, 4–17, Jan., 1953. 7 refs.

A statistical study is presented of the incidence of pulmonary tuberculosis in each of the metropolitan boroughs of London (excluding the City), based on the mortality rates from 1931 to 1948 and the (notified) morbidity rates from 1931 to 1939. These are first compared with the average rates for the County of London to obtain an indication of their relative levels and trends, and are then collated with various indices measuring the social and economic conditions of the 28 boroughs, including the " social index " (based on the occupations of the male population), population density, unemployment rate, mean weight of school-children, incidence of occupational risk, amount of open space, and the proportion of Irish-born persons in the population, and with Tuberculosis Dispensary attendances and expenditure per case. Correlation coefficients are calculated from which the direct and crossing influence of these factors on each other and on the primary rates may be assessed. It is recognized that some imponderables still remain, notably the effects of the war (with selective migration), the daily movement of three-quarters of a million workers to and from dormitory areas, and the changing industrial and social pattern of London, and that notification rates have been still further affected by the case-finding efforts of recent years.

The results show considerable heterogeneity amongst the various boroughs [the details of which can be appreciated only by studying the original paper]. Some decline in mortality from tuberculosis had taken place in every area during the period studied, but 4 boroughs (St. Pancras, Poplar, Shoreditch, and Stepney) appeared to lag behind the general rate of progress. War-time increases in mortality affected mainly those districts in which the pre-war rate had been high. The interdependence of the various environmental factors accounts for a number of apparent associations, and the author concludes that, in this type of investigation, little is to be gained by studying the effect of factors other than social class and housing density on tuberculosis mortality and morbidity. The association, here confirmed, of a high morbidity from tuberculosis with a poor social environment is still largely unexplained, and the writer modestly claims that his investigation " only adds to the pool of experience, not to any approach to finality " in the assessment of the relative importance of the various elements making up that environment.

R. J. Matthews

564. **An Examination of the Work of Local-authority Child-welfare Clinics**
J. T. A. GEORGE, C. R. LOWE, and T. MCKEOWN. *Lancet* [*Lancet*] **1**, 88–92, Jan. 10, 1953. 4 refs.

The authors have investigated the work done at 33 child welfare centres in Birmingham and at one in Coseley, Staffordshire. At the 33 centres in Birmingham, which has a population of 1,112,340, a total of 15 full-time and 26 part-time medical officers are employed and 64 clinic sessions are held each week. At Coseley, with a population of 34,414, one part-time medical officer attends 2 clinic sessions each week. At both places 2 health visitors are present at each session.

The distribution of proprietary foods at wholesale price, the routine weighing of the children, and the advice of the health visitors are considered by the mothers to be the most important services provided by these centres, some 44% of the mothers giving food purchase as a reason for attending. The medical services include immunization, routine examination, consultation, and treatment of minor ailments, 17% of the children at the Birmingham centres and 9% of these at Coseley being referred to the general practitioner or (in a very few instances) to hospital for treatment. The average number of children attending per session in Birmingham is 43 and the average number seen by the doctor is 17; at Coseley the respective figures are 52 and 14. About half of the mothers consider that attendance at the centre is preferable to attendance at a general practitioner's surgery, on the gounds of suitability (a crowded surgery being regarded as " no place for a child "), convenience (of both time and place), and accessibility of the clinic medical officer.

Although the preventive and curative medical services are the provinces respectively of the local authority and the general practitioner, 25% of the children attending these clinics are treated for minor disorders, the percentage referred to hospitals or general practitioners being 12. It is suggested that the advisory service of these clinics should be delegated to health visitors and the specifically medical duties undertaken by general practitioners under the National Health Service.

[The growth of the work of the child welfare centres over two generations has been such that the time may

well have come when some pruning is called for in the interests of economy. The figures given suggest that a considerable shift of the advisory function from the doctor to the health visitor has taken place. While general practitioners may, and do, conduct these clinics with complete success in country districts, it is open to question whether the reorganization suggested would be feasible in large cities.] *V. Reade*

INDUSTRIAL MEDICINE

565. **The Relative Value of Certain Building and Technical Materials as Regards their Permeability and Absorptive Capacity for Mercury Vapour.** (Сравнительная оценка некоторых строительных и технических материалов по их проницаемости и способности адсорбировать пары ртути)
C. F. YAVOROVSKAYA. *Гигиена и Санитария* [*Gigiena*] 35–39, No. 12, 1952.

A series of experiments have shown that saturation of building materials with water vapour diminishes their permeability to mercury fumes, while increased temperature increases it, the effect of temperature being more evident in finely porous material. The absorptive capacity of building materials and textiles depends upon the nature of their surface and on their dye content, dark dyes, many of which contain sulphur, absorbing more mercury than light ones. The absorptive capacity of walls and ceilings can be increased considerably by coating them with a plaster containing 20% powdered sulphur, and buildings so treated will, by absorbing the fumes of mercury, serve to purify the air and add to the safety of workers. The rougher the surface of the plaster, the more effective the absorption of mercury. Sulphur-containing paints and lacquers have been tested, and the best results obtained with oil paints with a basis of synthetic drying oil, probably because the very thin coat obtainable with such paints offers a closer contact between the sulphur and the mercury fumes.

L. Firman-Edwards

566. **Toxicity of 2:4-Dichlorophenoxyacetic Acid and 2:4:5-Trichlorophenoxyacetic Acid. A Report on their Acute and Chronic Toxicity in Dogs**
V. A. DRILL and T. HIRATZKA. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg.*] 7, 61–67, Jan., 1953. 7 refs.

Both 2:4-dichlorophenoxyacetic acid (2:4-D) and 2:4:5-trichlorophenoxyacetic acid (2:4:5-T) may act as plant hormones and selective herbicides and are used in weed control. This paper records a study of the acute and chronic toxicity of these two substances carried out at Wayne University, Detroit, on dogs. The LD50 of a single dose of 2:4-D given in a capsule by mouth was 100 mg. per kg. body weight, and that of 2:4:5-T was the same or a little higher. Anorexia and loss of weight followed large oral doses of both compounds, and death occurred between the second and ninth days after the capsule had been taken. With 2:4-D, the symptoms varied from a mild ataxia and stiffness in the hind legs to a definite myotonia. Occasionally there were signs suggestive of meningeal irritation or of a spinal or central lesion. There was sneezing, rubbing of the eyes, and diarrhoea, but no vomiting. With 2:4:5-T the symptoms were less marked, consisting in mild ataxia and slight stiffness of the hind legs. Death was due to pneumonia in several cases. At necropsy some inflammation of the intestinal mucosa was found, but other changes were non-specific, such as hepatic congestion.

Dogs receiving either 2:4-D or 2:4:5-T in doses of 10 mg. per kg. daily on 5 days a week for 90 days survived and showed no sign of poisoning, no change in body weight, in organ weights, or in blood count, whereas dogs receiving 20 mg. per kg. in one dose daily on 5 days a week all died. The symptoms of severe chronic poisoning were weakness, stiffness of the hind legs, ataxia, anorexia, difficulty in swallowing, and bleeding from the gums. No changes were found in the blood, except that in 3 dogs which died there was a terminal fall in the lymphocyte count.

M. A. Dobbin Crawford

567. **Emotional Stability in Colliery Workers**
A. HERON and D. BRAITHWAITE. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **10**, 27–31, Jan., 1953. 10 refs.

During an investigation at Manchester University into the incidence of rheumatic conditions among colliery workers (*Brit. J. industr. Med.*, 1952, **9**, 197), a small battery of objective tests of emotional stability, taking about 30 minutes, was applied to 184 workers (including 76 underground workers). All the men were between 40 and 50 years old. Five tests were included: (1) the Word Connection List, in which the subject chose between natural and bizarre alternatives; (2) the Maudsley Medical Questionnaire, a 40-item neuroticism inventory; (3) the Leg Persistence Test, in which the time the seated subject could hold out his leg fully extended was determined; (4) the Annoyances List, from which the subject was required to select annoyances to which he was susceptible out of a total of 60; and (5) the Finger Dexterity Test. From the results of these tests an " emotional instability score " between 1 and 9 was derived for each subject by statistical methods [for details of which the original paper should be consulted]. The mental health of the subjects was assessed by a physician as " well integrated " (39·6%), " doubtful, without definite symptoms " (49·7%), or " with signs or symptoms of mental ill-health " (10·7%) [no description of these signs and symptoms is given].

The product moment correlation between this simple rating and the nine-point emotional instability score was +0·3, which is significant. But on comparison of the distribution of cases among the physician's categories with the emotional instability scores, agreement was far from perfect, due mainly to the fact that the normalized test-battery scores placed many subjects in the " relatively unstable " half of the group who were classified by the physician as mentally healthy, there being far fewer cases of the opposite error. There was no correlation between the emotional instability score and the diagnosis

of rheumatism. The relation between the type of occupation and emotional stability was examined statistically. The instability scores of sedentary workers were found to be lower than those of part-time underground workers, which again were lower than those of full-time underground workers.

The authors conclude that the results of their investigation provide evidence in support of the contention of some other workers that there is " a greater prevalence of psychoneurotic handicap among underground workers ".

A. E. Bursill

568. **Some Psychological Conflicts Caused by Group Bonus Methods of Payment**

N. M. DAVIS. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **10**, 18–26, Jan., 1953. 5 refs.

The results are reported of an investigation, carried out at University College, London, into the effect on the morale and health of industrial workers paid " wage incentives ", that is, on the group bonus system. The author interviewed, singly, 382 men and 402 women, all of whom were paid on a group bonus system, and were employed in 5 factories making a variety of products. The investigation had the approval of the factory management and of the workers' representatives; only 0·4% of the workers refused information. Each individual was encouraged to talk frankly and to answer pre-determined questions aimed at elucidating his or her attitude to the pay system. About one-third of both men and women were satisfied with the system, another third were dissatisfied, and the remainder were neutral or divided in their attitude.

About 70% (including many workers whose general attitude was unfavourable) mentioned advantages of group bonuses—the extra earnings and the social benefits of the wage-levelling involved—but complaints of the inadequacy of the basic wage often accompanied such comment. Unfavourable comments were voiced by 80% of the workers, and chiefly concerned the relationship between individual effort and reward and the unpredictability of earnings. Such factors as production changes, variation in demand, breakdown allowances, and the fixed pace of some processes made bonus calculation so complicated that most workers could not estimate their progress, that is, they had no knowledge of the results and were consequently irritated by fluctuations in their weekly wage. The setting and subsequent adjustment of bonus standards also provided a target for criticism.

Social conflicts attributed to the system arose from hostile competition between groups and from suspected or real differences in individual capacity or willingness to work. Personal conflicts arose when the worker felt that the bonus system led to physical or mental strain, to a struggle between the desire for speed and the desire for quality, or had a deleterious effect on character. In no case had the factory medical officer played any part in formulating wage policy, and the author considers that, in view of the demonstrated effect of the bonus system on the worker's health and morale, it is desirable that he should do so.

H. F. King

569. **Age and Industrial Accident Rates**

H. F. KING and D. SPEAKMAN. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **10**, 51–58, Jan., 1953. 2 figs., 34 refs.

The dictum that older workers in industry are less prone to accidents than younger ones needs considerable caution in its application to any given body of workers. Without doubt, if older men do sustain injury by accident they are more likely to have a long period of disability and their mishaps are more likely to prove fatal. There are many other factors affecting the working of the general proposition but, " experience ", meaning the mere passage of time upon one particular job, does not of itself confer any real immunity against mishap in industry. The reason for this is very complicated. Not only is " experience " a very much overrated quality in human affairs generally, but the gaining of " experience " coincides with mental and physical deterioration, however energetically this process may be denied by the " experienced " worker.

G. F. Walker

570. **Occupational Skin Cancer in a Group of Tar Workers**

R. E. W. FISHER. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg.*] **7**, 12–18, Jan., 1953. 7 refs.

The author reports the result of a survey made by him of 241 men employed in a tar distillery in south London. Distillation of the tar was by the carbonization of coal in horizontal retorts. The aim of the survey was to observe the relation, if any, between the condition of the skin of each man and the occurrence of tar warts or epitheliomata, and in particular to determine whether proneness to these lesions could be determined before employment or early in the man's working life.

For the purpose of the inquiry, skin changes due to tar were classified as: (1) affections of the follicles; (2) acute tar erythema; (3) pigmentation and chronic erythema; (4) chronic tar dermatosis; and (5) tar warts and epitheliomata. Chronic tar dermatosis was further subdivided into: (*a*) alteration in skin texture; (*b*) simple plane warts; (*c*) rough hyperkeratoses; (*d*) freckles; and (*e*) capillary telangiectases. Rough hyperkeratoses, which show as hard, irregular-shaped, gray or black collections of keratinous material with the appearance of being laid on the skin, are fairly common in tar workers but, according to the author, they are not tar warts. Furthermore, he agrees with Bettley that it is not possible to differentiate clinically between a typical tar wart and an early squamous-celled tar epithelioma. The carrying out of the survey and its value were greatly helped by the fact that records of tar warts in this group had been kept throughout the preceding 25 years.

Of the 241 men, 66 had one or more tar warts, the total number being 422 warts. In one case warts occurred after only 11 months' exposure, whereas in another case the first wart did not appear until after 41 years' exposure. A workman with 26 years' exposure had had 63 warts, while another during 50 years had had 54. Investigation of the site showed that 70% of the warts occurred on the head and neck, and 28% on the forearm and hand, with

none on the palmar surface of the hand. In only 7 cases (1·7%) was the wart on the scrotum, a figure much lower than that given in other published series. Lastly the author found no evidence that fair-haired men are more prone to tar warts, as has been asserted, than are dark-haired men, nor does chronic " tar skin ", in his experience, necessarily precede the development of warts. There was, however, significant evidence to show that susceptibility to acute tar erythema is related to susceptibility to tar warts.

[Readers may be interested to note that the causes of death, with special reference to cancer of the lung, among the pensioners of this company have been analysed by Doll (*Brit. J. Industr. Med.*, 1952, **9**, 180)].

A. Meiklejohn

571. **The Aetiology of Caisson Disease.** (К этиологии кессонной болезни)

A. P. Brestkin. *Гигиена и Санитария* [*Gigiena*] 26–30, No. 12, 1952. 5 refs.

The author considers that the problem of the aetiology of caisson disease is not completely solved. The generally accepted theory, that the gas bubbles result from the release of nitrogen from solution in the blood owing to the fall in pressure, does not explain why the blood, which is better able than other tissues to get rid of excess of nitrogen, is the only site of gas formation. Another theory, propounded and developed by Yacobson, regards the lung alveoli and bowel as the source of minute bubbles which pass through the capillary walls into the blood stream, where they apparently act as foci for the formation of larger bubbles.

In experiments on dogs and rabbits the present author found that on decompression after subjection to pressures up to 1·8 atmospheres no bubbles were observed in the tissues of the animals; but if the pressure exceeded this figure bubbles were found in the synovial fluid, the lymph, and finally in the blood. When animals were subjected to a pressure of 20 to 25 mm. Hg for 2 to 3 hours focal lesions were found in the lungs. He does not consider that air can pass from the lungs into the blood-stream unless such lesions exist, and does not therefore accept the contention of Yacobson that this is a cause of caisson disease. He also points out that owing to surface tension the internal pressure in a bubble of nitrogen in the plasma is much greater than Yacobson calculates it to be, and that this tends to increase the rate of solution of nitrogen. In one of his experiments the femoral veins of dogs were severed and the ends united by a glass tube. When external pressure was reduced to 267 mm. Hg, corresponding to an altitude of 8,000 metres above sea-level, for a period of 30 minutes, not one gas-bubble was seen in the tube, nor were any seen on microscopical examination of the blood. It was also established that during decompression the blood in depots and the lymph are freed of nitrogen more slowly than the circulating blood. After decompression the partial pressure of nitrogen in bone marrow and fatty tissues may reach high values, and the blood circulating through them may absorb dangerous amounts of it, the formation of gas-bubbles proceeding rapidly; the same is true of the blood in depots, and these bubbles, entering the circulation, grow in size and give rise to massive gas-embolism.

[Two entirely different conditions are here confounded, one being caisson disease proper, which the " endogenous " theory suffices to explain, and the other being the lung trauma caused by sudden decompression which, as Leonard Hill showed, may lead to rupture of the alveolar walls and consequent gas embolism of the " exogenous " type.] *L. Firman-Edwards*

572. **Compressed-air Illness on Tyneside**

R. I. McCallum and D. N. Walder. *Lancet* [*Lancet*] **1**, 464–467, March 7, 1953. 4 refs.

573. **Coproporphyrinuria. Study of its Usefulness in Evaluating Lead Exposure**

S. S. Pinto, C. Einert, W. J. Roberts, G. S. Winn, and K. W. Nelson. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **6**, 496–507, Dec., 1952. 6 figs., 19 refs.

One of the " screening " methods hitherto used to discover workers suffering from lead poisoning has been that of direct measurement of the concentration of lead in the urine. To determine significant exposure to lead in 124 employees at a lead smelting plant the authors estimated the urinary excretion of coproporphyrin III by the improved method of Schwartz *et al* (*J. Lab. clin. Med.*, 1951, **37**, 843), which showed that the mean normal excretion was 160 μg. a day [about 11 μg. per 100 ml. of urine]. Of the 124 subjects, 32 were judged to have significant symptoms, but not one had the classical picture of lead poisoning, then or subsequently. Of these 32, 27 (84%) excreted more than 40 μg. of coproporphyrin per 100 ml. of urine, as compared with 21 (23%) of the 92 who had no symptoms. Estimation of the urinary excretion of lead gave less definite results, but estimation of the concentration of lead in the blood showed that in 26 (81%) of the 32 patients with symptoms and in 30 (33%) of the 92 without symptoms the blood level was over 95 μg. per 100 ml. The distribution of cases according to the basophilic aggregation count appeared to be less definite, while the stippled-cell count was of little value. The 4 patients with the most definite symptoms were among the 7 with the highest urinary excretion of coproporphyrin and among the 9 with the highest urinary excretion of lead. In the series as a whole there was little correlation between a raised concentration of lead in the blood and the urinary excretion of coproporphyrin, but there was a correlation between the latter and the urinary excretion of lead. The authors consider that in lead poisoning estimation of the coproporphyrin content of the urine is of more value than other screening methods. No association between blood pressure and years of exposure was observed.

[The symptoms thought to be attributable to lead are neither listed nor discussed. On the validity of these, always a debatable matter, hangs the whole of this comparative study.] *J. N. Agate*

See also Dermatology, Abstract 544.

Toxicology

574. **Localization of the Enzymatic Block in Kidneys of Rats Treated with Fluoroacetate**
H. BUSCH and V. R. POTTER. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **81**, 172–175, Oct., 1952. 1 fig., 8 refs.

Previous experiments having shown that a " fluorotricarboxylic acid " formed from fluoroacetate inhibits aconitase *in vitro*, the authors studied the oxidative metabolism of citrate and other Krebs-cycle acids by rat-kidney homogenate *in vitro* following the intraperitoneal administration of 5 mg. of fluoroacetate per kg. body weight *in vivo*. Citrate accumulation in the tissues was taken as evidence of poisoning. Aconitase activity was determined in kidney homogenates in the presence of *cis*-aconitate, cysteine, and ferrous ammonium sulphate. Aconitase and oxidative activity were determined in the same preparation, using *cis*-aconitate as substrate and arsenite (0·0002M) to depress α-ketoglutarate oxidation.

It was found that citrate oxidation by rat-kidney homogenate poisoned with fluoroacetate was markedly depressed, whereas oxidation of other substrates of the Krebs cycle, including *cis*-aconitate, was only slightly depressed. Conversion of *cis*-aconitate to citrate was not markedly affected under conditions in which the reverse reaction was markedly inhibited. *J. Dawson*

575. **Antidotal Efficacy of Vitamin B_{12a} (Hydroxocobalamin) in Experimental Cyanide Poisoning**
C. W. MUSHETT, K. L. KELLEY, G. E. BOXER, and J. C. RICKARDS. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **81**, 234–237, Oct., 1952. 8 refs.

The addition of cyanide ions to a solution of vitamin B_{12a} (hydroxocobalamin) results in the formation of vitamin B_{12} (cyanocobalamin). The cyano- group is tightly bound to the cobalt atom and the process is apparently irreversible, for vitamin B_{12} is non-toxic to mice even when given in doses up to 1,600 mg. per kg. body weight intravenously and intraperitoneally, a dose which contains the equivalent of 32 mg. of cyanide ion per kg., which is about 8 times the LD100 dose. These observations suggest that vitamin B_{12a} might be of value as an antidote to cyanide, and this has been confirmed by the authors in a series of experiments on mice carried out at the Merck Institute, Rahway, New Jersey, in which it was shown that vitamin B_{12a}, administered intravenously, is capable both of preventing and of reversing the effects of the intraperitoneal injection of aqueous solutions of potassium cyanide.

For prophylaxis, a dose of 50 or 250 mg. of vitamin B_{12a} per kg. given 20 seconds before the cyanide injection gave adequate protection against doses of 5·5 to 8·0 mg. per kg. In treatment an intravenous dose of 250 mg. of vitamin B_{12a} per kg. given within one or two minutes, or of 100 mg. per kg. within one minute, of the intraperitoneal injection of 10 mg. of potassium cyanide per kg. (a lethal dose) caused the immediate disappearance of respiratory distress and convulsions and prevented death. Given 6 to 8 minutes after the injection of potassium cyanide, vitamin B_{12a} was ineffectual. However, mice " apparently dead " of cyanide poisoning reacted dramatically to the injection of vitamin B_{12a} within 2 to $3\frac{1}{2}$ minutes of the cyanide injection, 7 out of 21 recovering.

In a study of the metabolism of cyanide and vitamin B_{12a} each of 6 mice was poisoned by the intraperitoneal injection of 10 mg. of potassium cyanide per kg., and approximately one minute later each was given an intravenous injection of 100 mg. of vitamin B_{12a} per kg. The urine was collected during the next $2\frac{1}{2}$ hours and it was found that 9·6% of the cyanide given was excreted in the urine during this period in the form of cyanocobalamin, 0·7% as free cyanide, and 3·5% as thiocyanate. *M. A. Dobbin Crawford*

576. **Morphological Alterations in the Brain after Intoxication with Parathion (*p*-Nitrophenyldiethylthiophosphate).** [In English]
H. SIEDEK and H. THALER. *Archives internationales de pharmacodynamie et de thérapie* [*Arch. int. Pharmacodyn.*] **91**, 194–201, Sept. 1, 1952. 5 figs., 8 refs.

In the last few years " parathion " has been widely used as an insecticide in agriculture. In acute poisoning with this insecticide central nervous symptoms predominate. The present study, made at the First Medical Clinic, Vienna University, records the effect of acute and chronic poisoning in dogs, 7 of which were given parathion in doses varying from 8 mg. per kg. body weight to a total of 98 mg. per kg.; in the latter case the dog survived for 22 days with the help of atropine, which eliminated acute toxicity. Animals which died from parathion poisoning showed extensive hyperaemia and haemorrhages in all parts of the brain and spinal cord. Degeneration of ganglionic cells was also present within 30 hours after the first dose of parathion, and after 22 days degeneration of the myelin sheaths was noted. These changes do not appear to be related to the cardiovascular disturbances. *Derek R. Wood*

577. **Organic Phosphate Insecticide Poisoning. Report of Two Cases due to Parathion with Recovery in One**
H. R. CHAMBERLIN and R. E. COOKE. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **85**, 164–172, Feb., 1953. 26 refs.

578. **Poisoning by Methyl-parafynol (Dormison). Fatal Suicidal Overdose of 3-Methylpentyne-ol-3, a New Hypnotic**
R. M. CARES, B. NEWMAN, and J. C. MAUCERI. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **23**, 129–133, Feb., 1953. 14 refs.

Anaesthetics

579. **Bloodletting during Operation to Diminish Bleeding**
B. L. Borri and F. Natellis. *Current Researches in Anesthesia and Analgesia* [*Curr. Res. Anesth.*] **32**, 6–18, Jan.–Feb., 1953. 5 figs., 17 refs.

The authors, working at the University of Rome, describe their attempts to reduce haemorrhage during experimental surgery in dogs by the production of hypotension. The method chosen was blood-letting and re-infusion of blood by a cannula placed in the common carotid artery. The method was found to be of value in operations on the heart and liver. The authors consider, however, that the quantity of blood withdrawn should not exceed one-quarter of the circulating blood volume.

The mortality in this series of 24 dogs was high (12 of the animals died), but this was due in part to imperfections of technique. *Ronald Woolmer*

580. **Some Clinical Observations on the Use of " Surital " Sodium in Combination Anesthesia**
H. S. Phillips. *Current Researches in Anesthesia and Analgesia* [*Curr. Res. Anesth.*] **32**, 56–61, Jan.–Feb., 1953. 1 fig., 4 refs.

" Surital " is a thiobarbiturate which is an analogue of quinalbarbitone (" seconal ") and differs from thiopentone in having an allyl group in place of the ethyl side-chain. The author reports a series of 337 cases in which the sodium salt of surital was given, mostly in 2·5% solution, in situations exactly comparable to those in which thiopentone is commonly used—for short procedures as the sole anaesthetic agent and for longer operations as a precursor to other anaesthetics. The impression was gained that surital is appreciably more potent than thiopentone and that, since a smaller dose can be used, recovery is more rapid. It appeared that laryngeal irritability was less prominent than is often the case with thiopentone. *Donald V. Bateman*

581. **Use of Local Analgesia in Septic-finger Surgery at a Teaching Hospital**
P. E. B. Holmes and D. J. C. Graff. *British Medical Journal* [*Brit. med. J.*] **1**, 255–257, Jan. 31, 1953. 1 fig., 2 refs.

The authors, at King's College Hospital, London, studied the effect of local analgesia in 256 cases in which operation was performed for septic finger between February and July, 1952. [The surgical technique, which is described in greater detail than the method of analgesia, conformed to accepted practice.]

During the first two months of the period analgesia with a 2½% solution of procaine without adrenaline was induced by the standard technique of deposition at the base of the proximal phalanx. This method was later superseded by an approach from the dorsum of the hand on each side of the knuckle: the dorsal skin between the knuckles was stretched and a very fine needle introduced; the needle was then directed distally and forwards, close to the proximal phalanx, and the solution deposited near the digital nerve as it leaves the palm just distal to the deep transverse ligament. Before the needle was withdrawn it was re-directed across the knuckle to block the dorsal nerves and raise a weal at the site for injection on the opposite side. It was found that 6 ml. of solution was usually more than enough. An interval of at least 5 minutes, and preferably 10 minutes, was allowed for the block to become effective.

The authors have compared the results obtained in 153 of these cases with those obtained in 130 cases treated by operation during the previous year under general anaesthesia. This comparison revealed an average reduction of 3 days in postoperative disability time when local analgesia was employed. The authors conclude that " local analgesia is definitely superior to general anaesthesia for infections of the fingers ". *Michael Kerr*

582. **Controlled Hypotension by a Thiophanium Derivative**
I. W. Magill, C. F. Scurr, and J. B. Wyman. *Lancet* [*Lancet*] **1**, 219–220, Jan. 31, 1953. 1 fig., 6 refs.

The authors discuss the limitations and disadvantages of penta- or hexa-methonium bromide for the deliberate production of hypotension during anaesthesia. In their work as anaesthetists at Westminster Hospital, London, they have found that the methonium compounds are satisfactory only if given in one large initial dose, and that repeated smaller injections are less effective. They also found that very young or thyrotoxic patients are resistant to the effects of pentamethonium. Furthermore, they point out that the termination of the hypotension by the administration of antagonistic drugs does not necessarily indicate a direct physiological reversal of the hypotension.

A new ganglionic blocking agent was described in 1949 by Randall *et al.* (*J. Pharmacol.*, 1949, **97**, 48). It is D - 3:4 - (1′:3′ - dibenzyl - 2′ - ketoimidazolido) - 1:2 - trimethylene thiophanium D-camphor sulphonate, known also by its code number, Ro 2-2222, or as " arfonad ". The present authors recently had the opportunity to test this drug in 5 surgical cases. The drug is given by intravenous drip, the drip solution containing 1·0 mg. of the drug per ml. and being given at the rate of 3 ml. per minute. The blood pressure was readily controllable by varying the rate of drip, recovered rapidly after the drip was stopped, and remained very stable during several hours' postoperative observation. No side-effects or complications were encountered, and in every case results were highly satisfactory. The drug appears to overcome the disadvantages of the methonium compounds and if these early hopes are fulfilled it may well supplant other hypotensive agents. *W. Stanley Sykes*

Radiology

583. **Further Studies of the Mechanism of Pulmonary Clearance of Prodigiosin in Normal and X-irradiated Rabbits**
G. V. TAPLIN, J. S. GREVIOR, C. FINNEGAN, A. DUNN, and P. NOYES. *Annals of Allergy* [*Ann. Allergy*] **11**, 1–11, Jan.-Feb., 1953. 4 figs., 25 refs.

In continuation of their earlier experiments (*Ann. Allergy*, 1952, **10**, 397; *Abstracts of World Medicine*, 1952, **12**, 532) at the School of Medicine, University of California, on the removal of dust containing the dye prodigiosin from the lungs of normal and *x*-irradiated rabbits the authors have now studied the removal of colloidal prodigiosin given by intravenous injection. In rabbits whose whole body was exposed to a dose of 800 r the insoluble foreign particles were removed more quickly than in animals which were not irradiated. This removal by phagocytic action was depressed for varying intervals up to 14 days, after which an acceleration of phagocytosis occurred; the highest mortality was observed during the period of depression. The removal of the dye from the reticulo-endothelial system, for which the only mechanism was phagocytosis, was much slower and less complete than that of prodigiosin dust from the lungs by ciliary action and increased mucous secretion. These findings are discussed in relation to inhalation hazards in atomic warfare and in industry.

H. Herxheimer

RADIOTHERAPY

584. **Roentgen Therapy of Peritendinitis Calcarea of the Shoulder. A Study of 220 Cases with Late Results**
E. A. KRATZMAN and R. S. FRANKEL. *Radiology* [*Radiology*] **59**, 826–830, Dec., 1952. 13 refs.

The 220 cases of peritendinitis calcarea reviewed in this paper from the Roosevelt Hospital, New York, were divided into 107 acute cases of not more than one week's duration, 23 subacute cases of 1 to 4 weeks' duration, and 90 chronic cases of more than 4 weeks' duration. Follow-up was by letter and was successful in 157 cases out of 195 contacted (80·5%). The series comprised 119 male and 101 female patients, and the right shoulder was involved rather more often than the left; there were 17 bilateral cases. The diagnosis was confirmed by radiography of the shoulder in only 150 cases. The irradiation factors were: 200 kV, 15 mA, 0·5 mm. Cu. with 1·0 mm. aluminium filtration, and a skin–target distance of 50 cm. The size of the field was 10×10 cm., and the dose was 150 r in air every other day to a total dose of 450 to 600 r.

Of the acute cases 91% eventually obtained complete relief, but in only 52% was this relief rapid. The results in the subacute and chronic cases were less good, 69% of the former and only 52% of the latter eventually obtaining complete relief. The authors' conclusions are that the immediate response is usually remarkable and most gratifying, but that complete relief is often a gradual process. They consider that the results are permanent.

E. Stanley Lee

585. **The Injection of Colloidal Radioactive Gold into the Portal Circulation.** (Or colloïdal radio-actif introduit par voie intraveineuse portale. Étude préliminaire, expérimentale et clinique)
J. CLOSON. *Journal belge de radiologie* [*J. belge Radiol.*] **35**, 617–628, 1952. 2 figs., 5 refs.

The author has investigated, at the University of Liège, the therapeutic possibilities in cases of metastatic carcinoma of the liver of the injection into the portal vein of colloidal radioactive gold (^{198}Au) which emits β rays of 0·96 MeV and γ rays of 0·411 MeV, its period of disintegration being 2·69 days and the resultant product being mercury. Using rabbits in preliminary experiments, he exposed a mesenteric vein by laparotomy and injected a dose of the gold preparation equivalent to 3·5 millicuries. During the 5 days following this operation the faeces and urine were collected, and on the sixth day the animal was killed by bleeding. The blood thus obtained, the urine from the bladder collected after death, and various organs were weighed and the radioactivity of these specimens and those collected during the preceding 5 days assessed by means of a Geiger counter. It was found that the liver retained approximately 75% of the radioactivity of the ^{198}Au originally injected, the bone marrow 1·5%, the muscles 0·2% and the skin and lungs 0·1%. The proportion excreted in the urine and faeces during the 5-day period was of the order of 1·4%. It is pointed out that although the quantity retained in the bone marrow was small, its importance should not be underestimated in view of the radiosensitivity of this tissue.

The author then reports the results of administration of colloidal ^{198}Au into the portal circulation in 2 patients with multiple hepatic metastases. In the first case a dose of approximately 100 millicuries of ^{198}Au in colloidal form was injected into an epiploic vein. By means of a Geiger counter it was ascertained that a large amount of the gold had been retained by the liver. The injection was followed a month later by a liver biopsy, from which it was calculated that 14% of the amount originally injected was still present. During the first fortnight after the injection the urinary excretion of ^{198}Au was 2·2% and that in the faeces 0·4% of the amount originally injected. The salivary glands excreted 0·05% during the same period. As a result of this treatment the liver decreased considerably in size and became painless, although the primary tumour, an epithelioma of the bronchus, remained unaffected. The patient had no anaphylactic symptoms, no radiation symptoms, and no

signs of intoxication by gold. He died 6 weeks after the injection from cardio-respiratory complications of the primary disease, and there was no post-mortem examination. The second patient was suffering from carcinoma of the gall-bladder with metastases in the liver. At laparotomy the inoperability of the primary lesion was confirmed, and a dose of 85 millicuries of ^{198}Au was injected into the portal vein. After 2 weeks, 75% of the original radioactivity was retained by the liver, and during that time the kidneys excreted 0·9%, the alimentary tract 0·26%, and the salivary glands 0·1%. There was considerable decrease in size of the liver, which was no longer painful, and also a reduction of pruritus. The patient's condition did not deteriorate in any respect, and a good palliative effect was obtained. The patient died 2 months after the injection, but no further information was available. The author admits that in neither case had the treatment any effect on the primary tumour, but he stresses the fact that in both cases the carcinoma was of low radiosensitivity. He recommends the use of colloidal radioactive gold as a very potent palliative measure in cases of metastatic disease of the liver.

W. J. Czyzewski

586. **The Two Million Volt Van de Graaff Generator Installation Designed for Rotation Therapy at the Royal Cancer Hospital**

B. M. WHEATLEY, P. R. STEED, E. W. SAVAGE, J. H. KING, E. W. FORSTER, H. J. HODT, I. R. JONES, and D. W. SMITHERS. *British Journal of Radiology* [*Brit. J. Radiol.*] **26**, 57–58, Feb., 1953. 1 fig.

587. **Treatment of Advanced Carcinoma of the Bladder with Two-million-volt Rotation Therapy**

J. E. STAPLETON. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol.*] **4**, 207–210, Jan., 1953. 5 figs., 1 ref.

An interim report is presented, after a year's experience, on the treatment of carcinoma of the bladder with the 2-million-volt Van de Graaff *x*-ray machine at the Royal Cancer Hospital, London. During this time 18 cases have been treated, most of those selected being cases of infiltrating carcinoma clinically limited to the bladder and paravesical fat. Two patients with advanced disease with fixation to the pelvic wall were also treated but received little benefit, and cases of this type would now be regarded as unsuitable. One patient with a suprapubic fistula was unable to complete treatment, and this also would now be considered a contraindication.

A rotating treatment table was used, the patient being rotated through an arc of 300 degrees only in order to spare the perineum and testes. The tumour dose varied from 5,500 to 6,500 r in 6 weeks, the maximum skin dose being between 1,200 and 2,400 r. No severe skin reactions were seen, even in fat patients, so that it was possible to start treatment even in the presence of recent suprapubic scars. Bladder symptoms—frequency, dysuria and strangury—were as common as after conventional *x*-ray therapy, but rectal symptoms were very mild and there were no symptoms of radiation sickness.

Only one case, the first, showed no regression, and here total cystectomy was successfully carried out. Eight patients showed no sign of a tumour on cystoscopy and were free from symptoms at the time of the report, whereas in 3 cases treated recently the tumour was still present, but regressing. There have been 4 deaths, including the 2 patients with advanced disease mentioned above, a third patient dying of pyelonephritis, and a fourth of widespread metastases, although the bladder remained free from disease. *E. Stanley Lee*

See also Otorhinolaryngology, Abstract 472.

RADIODIAGNOSIS

588. **Roentgenographic Diagnosis of Tumours of the Glomus Jugularis**

P. A. RIEMENSCHNEIDER, G. D. HOOPLE, D. BREWER, D. JONES, and A. ECKER. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **69**, 59–65, Jan., 1953. 8 figs., 8 refs.

The glomus jugularis is a small structure situated in the adventitia of the jugular bulb, just below the middle ear. It is histologically identical with the carotid body, and is thought to have a similar function. Over 30 cases of tumour of this body have been described in the literature. Glomus tumours arise above the dome of the jugular bulb, erode the floor of the middle ear, which they fill and then break through the tympanic membrane to appear as a bleeding polyp in the external auditory meatus. Later there may be massive destruction of the petrous bone, with involvement of cranial nerves, pressure on the brainstem, and extension into the nasopharynx. The radiological features are of sclerosing mastoiditis in the early stages, and extensive destruction of the lower part of the petrous pyramid later.

In this paper the authors describe 2 cases seen at New York Medical Center, Syracuse, New York. The first patient, a man of 24, presented with unilateral deafness and tinnitus. Radical mastoidectomy disclosed a very vascular tumour; this was partly removed, and 1,000 r postoperative irradiation was given. Three years later there was extensive recurrence, with involvement of the cranial nerves and papilloedema. Radiographs showed massive destruction of the lower part of the petrous bone, and a vertebral angiogram demonstrated filling of the tumour vessels.

The second case was that of a woman aged 52 with a long history of aural discharge and several previous operations for removal of tumour. Radiographs demonstrated a mass in the postnasal space, with extensive destruction of the petrous bone and middle fossa. Further removal was attempted and 100 mg. of radium was inserted for 10 hours. When the patient was seen 9 months later the ear was almost dry and there was a marked decrease in the swelling.

D. E. Fletcher

589. **The Value of Tomography in Examination of the Intrapulmonary Bronchi.** [In English]

H. LODIN. *Acta radiologica* [*Acta. radiol. (Stockh.)*] Suppl. 101, 1–109, 1953. 47 figs. Bibliography.

590. **Carcinoma of the Breast. Roentgenographic Technic and Diagnostic Criteria**
J. GERSHON-COHEN and H. INGLEBY. *Radiology* [*Radiology*] **60**, 68–76, Jan., 1953. 9 figs., 29 refs.

It is first suggested that in view of improved radiological technique *x*-ray examination should be a routine procedure in the diagnosis of carcinoma of the breast. The authors then describe the technique adopted at the Albert Einstein Medical Center, Philadelphia.

Lateral and tangential views of each breast are taken with a non-screen, industrial, fine-grain film, the factors being 30 to 38 kV and 200 to 400 mA. For the lateral view a cone from which one sector is cut out is used and the breast compressed against the film through the medium of a thin plastic sheet. Smaller cones are used for "local" views. Considerable technical skill is required, but the authors state that with adequate films and a knowledge of the patient's history and the clinical findings an accurate diagnosis may be expected in 90 to 95% of cases.

In their experience, when a tumour is malignant the size of the mass as determined radiologically is smaller than the size as determined clinically; the tumour is also denser than the surrounding tissue, which shows a blurred and distorted outline, and has an irregular and spiculate margin. Very fine, extensive, punctate calcification may occur. Other features are: local thickening of the skin, thickening of the normal trabeculae, and increased vascularity in parenchyma and subcutaneous fat.

In a brief discussion of the differential diagnosis, the authors state that benign tumours and cysts have a smooth outline, there is no increased vascularity, and although surrounding structures are displaced, there is no trabecular thickening. Haemorrhage from intracystic papilloma may make the cyst unusually distinct. In secretory cystic disease an irregular mass may be seen with surrounding extensions, but the latter follow the pattern of the trabeculae and the mass is indefinite clinically. Breast abscess resembles the diffuse type of carcinoma, but the diagnosis is usually clinically obvious.

Kenneth A. Rowley

591. **Full-column Technic in Lumbar Disk Myelography**
L. MALIS, C. M. NEWMAN, and B. S. WOLF. *Radiology* [*Radiology*] **60**, 18–28, Jan., 1953. 13 figs., 8 refs.

The limitations of myelography in lumbar disk lesions, especially when small amounts of opaque medium are used, are discussed and a new technique, employed at Mount Sinai Hospital, New York, in which relatively large quantities of "pantopaque" are used, is described. The authors found that in 50% of cases, with the patient in the erect position, 6 ml. of pantopaque reached the body of L4 and that in the remaining cases, 9 or 12 ml. was required; on a few occasions as much as 24 ml. was injected "without ill-effect". Screen examination was reduced to a minimum, and antero-posterior, lateral, and 45-degree oblique films were taken. If no lesion was observed, then 30-degree and 60-degree oblique films were examined before the medium was removed.

It is admitted that small defects within the subarachnoid space may be masked by the use of large amounts of medium, but on the other hand any impingement on the column of pantopaque from without, as by disk lesions, is readily seen. Radiographs taken in 6 cases are reproduced.

Kenneth A. Rowley

592. **The Radiological Diagnosis of Abscess of the Greater Sac of the Peritoneal Cavity.** (Radiodiagnostic des abcès de la grande cavité péritonéale)
C. OLIVIER, J. HUGUIER, and N. ARVAY. *Presse médicale* [*Presse méd.*] **61**, 101–104, Jan. 28, 1953. 14 figs.

The authors draw attention to certain radiological features which may be seen in cases of abscess within the peritoneal cavity. They describe in detail the findings in a patient with an appendicular abscess, and give other illustrative examples of such cases. The features which they emphasize are: (1) the tendency to gaseous distension, especially of the small intestine; (2) the filling defect produced in the intestine by the mass; (3) the occasional presence of gas and fluid within the abscess cavity; and (4) the blurring of the parallel soft-tissue shadows in the lateral aspects of the abdomen.

[The radiographs reproduced demonstrate clearly the points which the authors make, and their article is useful in that it emphasizes the value of taking plain films of the abdomen of patients suffering from acute or subacute abdominal infections.]

R. A. Kemp Harper

593. **The Diagnosis of Volvulus of the Cecum**
H. L. ABRAMS and W. A. WASS. *Radiology* [*Radiology*] **60**, 36–45, Jan., 1953. 10 figs., 34 refs.

In this paper, from Stanford University and County Hospital, San Francisco, the radiological criteria for diagnosis of volvulus of the caecum are described, together with 7 proved cases, in which the age of the youngest patient was 40. The term volvulus of the caecum implies a twisting of the bowel, which produces luminal occlusion, resulting in the clinical picture of acute intestinal obstruction, but without any characteristic features. The authors describe the embryonic development of the intestine, indicating how an abnormal mobility of the caecum is usually due to failure of mesenteric fusion in the region of the ascending colon. Radiologically the diagnosis is based on the following characteristic features. (1) On the plain film a markedly dilated loop of large bowel is seen with its axis directed towards the right iliac fossa; there is no gas in the transverse or descending colon. Dilated loops of the small bowel are always present. (2) A barium-enema examination reveals obstruction in the region of the ascending colon or hepatic flexure.

The literature is discussed and radiographs for each of the 7 cases are reproduced.

[Although plain films are of considerable value in determining the necessity for operation and in diagnosis, it seems doubtful whether the additional diagnostic aid of a barium-enema examination is justified in most cases.]

Sydney J. Hinds

See also Infectious Diseases, Abstract 357; Gastroenterology, Abstract 406; and Urogenital System, Abstract 480.

History of Medicine

594. William Harvey and the Early Days of Blood Transfusion

J. M. GRAHAM. *Edinburgh Medical Journal* [*Edinb. med. J.*] **60**, 65–76, Feb., 1953

Himself a pioneer in the technique of blood transfusion, the author shows, in his Oration delivered at the 157th Harveian Festival in 1952, how this procedure, which has been the means of saving countless lives, was introduced as a natural consequence of the discovery of the circulation of the blood. " By showing the value of the experimental method in investigating function, Harvey did for physiology what Vesalius had done for anatomy ". The new discovery " at once made logical the endeavour to replace blood which had been lost by the transfusion of blood from another individual ". This method of treatment has been envisaged from time immemorial, but it did not become a practical proposition until the time of Christopher Wren, who, like Leonardo da Vinci before him, was a man of amazing versatility. In 1657, almost thirty years after the publication of Harvey's immortal treatise, *De motu cordis*, Christopher Wren, at that time a student at Oxford, injected into the veins of a large dog a solution of opium, thus proving the practicability of intravenous therapy and showing the way to the successful transfusion of blood. A few years later, also at Oxford, Richard Lower performed the first successful transfusion of blood, connecting the carotid artery of one dog to the jugular vein of another. Details of each of those experiments were published by Robert Boyle, and in the *Diary* of Samuel Pepys, under the date Nov. 14, 1666, there is a reference to the experiments and even a suggestion that the method " may be of mighty use to man's health for the amending of bad blood by borrowing from a better body ". In 1667 Lower performed blood transfusion in man for the first time in England. A lamb provided the blood, its carotid artery being connected by a long silver tube with the vein of the patient, a young man of 22 suffering from some form of mental disturbance. The transfusion was successful, but although a few other striking successes followed, the danger of the procedure soon became evident, and as it was not realized that this was largely due to giving dissimilar blood the operation fell into disrepute.

The next step was not taken until 1818, when James Blundell, a London obstetrician, performed the first transfusion of blood from one human being to another. He proceeded with the greatest caution, choosing at first patients who were already moribund, or even dead, yet 4 of the 10 patients he treated were restored by the transfusion and recovered. The employment of vascular suture and the use of paraffined cannulae were further advances, but the operation remained uncertain in its results until Landsteiner, in 1901, discovered that the erythrocytes of one individual were frequently agglutinated by the serum of another of the same species, though it was not until 10 years later that the various blood groups were identified and the agglutination tests worked out. Another advance was the discovery in 1915 by Lavisohn and Agote almost simultaneously that the addition of sodium citrate to the blood would prevent coagulation and that blood so treated could safely be injected. The introduction of the citrate method and of the tests for compatibility at last made transfusion a safe, simple, and reliable procedure. All those advances arose out of Harvey's genius, and " the long history of transfusion illustrates how progress in the application of a procedure must sometimes patiently wait upon new facts and discoveries in science or in medicine which, taken by themselves, may appear to have little bearing on the problem under consideration ".

[Every Harveian Orator of to-day is faced with a difficult task. All that Harvey wrote or did, the background of his career, the effect of his discovery, the revolution he wrought in physiology, and almost every other detail concerning the man and his work—all that has already been discussed by generations of previous Orators. The author is therefore to be congratulated on having discovered a new route of approach to Harvey, and his Oration gives an excellent account of the rise and progress of blood transfusion, and its dependence upon Harvey's discovery. It would have been even more valuable had a bibliography been added, but that is a minor defect.]

Douglas Guthrie

595. The Place of William Withering in Scientific Medicine

J. F. FULTON. *Journal of the History of Medicine and Allied Sciences* [*J. Hist. Med.*] **8**, 1–15, Jan., 1953. 1 fig., 14 refs.

In this biography of William Withering and assessment of his contribution to medicine, the author remarks that " there are few more striking examples of how seed of great potentialities was nourished by the rich soil in which it was cast ". Withering was born in Shropshire in 1741, his formative years coinciding with a revival of learning which affected the Midlands rather than the academic centres of Britain. Many were there who declined to embrace the new regime of the Church, and it was in the Nonconformist areas that free-thinking dissenters, united by a common love of science, formed groups for discussion and study. In Birmingham the Lunar Society was one such group, the members of which included Erasmus Darwin, Joseph Priestley, John Baskerville, James Watt, William Withering, and others, and which met each month at full moon, so that the members might be lighted homeward. The society flourished for about forty years and exercised a far-reaching influence. Withering arrived in Birmingham in 1775. He had studied in Edinburgh when the University was at the height of its fame, and among the teachers who specially impressed him there were Robert

Whytt and William Cullen. Little is known of his student life, but that he followed Scottish custom and tradition is apparent from the fact that he played golf and also learned to play the bagpipes. He was awarded the M.D. degree in 1766 for a thesis entitled *De angina gangraenosa* [a translation of which is published immediately after the present paper]. After continuing his studies in London under William Hunter and on the Continent, Withering settled in Stafford, then a small country town. He remained there for nine years, and it was during this period that he was drawn to the field of botany, a study doubtless fostered by his marriage to a keen botanist, Miss Helena Cooke. So seriously did he pursue this avocation that he was able eventually to write the two-volume treatise on British plants which became a classic. In Birmingham, to which city he later moved on the suggestion of Erasmus Darwin, he soon built up a large practice, yet although he spent much of every day travelling many miles in horse-drawn vehicles over bad country roads, he found time to make elaborate clinical notes and to continue his botanical studies. But, like many hard workers of that time, he fell a victim to tuberculosis, and despite the fact that he was able to prolong his days on earth by living in the country and by spending several winters in Portugal, his health gradually declined and he died in 1799 at the age of 58.

The author reminds us that Withering was not only an ardent botanist: he was also eminent as a mineralogist and chemist, in which field his attention was focused upon barium salts, and it was after him that barium carbonate received its name of Witherite. But of course the achievement for which he is generally remembered today was his discovery of the therapeutic value of digitalis (or rather, of foxglove) in cases of dropsy. The well-known story of the discovery of this remedy illustrates the occasional value of plants already established as folk-remedies. Withering obtained the secret from an old woman in Shropshire " who had sometimes made cures after the more regular practitioners had failed ". After a careful study of the preparation and dosage of the remedy, he was able to formulate rules for its administration, and in 1785 he published his monograph, *An Account of the Foxglove*, a classic now rare and valuable, in which were recorded 163 of his own cases. Some account is given of the unfortunate estrangement between Withering and Erasmus Darwin over the question of priority for the discovery. It appears that Darwin had advised the use of digitalis for dropsy at an earlier date than did Withering, but it was certainly Withering who inaugurated the systematic use of the drug. He won high honours, becoming a Fellow of the Royal Society, of the Linnean Society, and of the Medical Society of London. His house at Birmingham became a centre of pilgrimage for many—scientists as well as physicians. The place of Withering in scientific medicine is firmly established. *Douglas Guthrie*

596. **A Translation of William Withering's *De angina gangraenosa***

C. D. O'MALLEY. *Journal of the History of Medicine and Allied Sciences* [*J. Hist. Med.*] **8**, 16–33, Jan., 1953. 11 refs.

597. **Benjamin Guy Babington, M.D., F.R.C.P., F.R.S. (1794–1866)**

T. G. WILSON. *Journal of Laryngology and Otology* [*J. Laryng.*] **67**, 90–97, Feb., 1953. 5 figs., 11 refs.

Manuel Garcia, the Spanish teacher of singing, has long been credited with the introduction of the laryngoscope, but it appears that he was forestalled by Benjamin Guy Babington by some 26 years. The Babington family history can be traced back to Norman times. Benjamin's father, William, was a member of a branch of the family long settled in Ireland. A man of versatile ability, he was physician to Guy's Hospital, a noted mineralogist, a Fellow of the Royal Society, and a prime mover in the foundation of both the Geological Society and the Hunterian Society. Young Benjamin was born in Guy's Hospital, from which he derived his middle name. After serving for a short period as a midshipman in the Royal Navy, Benjamin continued his education at Cheltenham and Haileybury. He was subsequently appointed to the Indian Civil Service and spent ten years in India, where he made a considerable reputation as an Orientalist. His health broke down however and, his wife having died, he returned to England with his children and decided to take up the study of medicine. He was appointed assistant physician to Guy's in 1837 and was full physician from 1840 to 1855. Bright (who was his brother-in-law), Addison, and Hodgkin were his colleagues and friends. In 1855 he retired in order to devote more time to the work of the Epidemiological Society, which he had founded. He died in 1866.

The development of the laryngoscope was not the work of one man but of many. In 1807 Bozzini of Frankfurt-am-Main described a lamp to which was attached a hollow tube containing a mirror. This instrument had some resemblance to modern rectal and vaginal specula and was not well adapted to laryngological work. In 1827 Senn of Geneva described a small instrument which seems to have been very similar to the modern larngoscope, but it appears never to have been put to serious practical use. Babington's instrument was exhibited at the Hunterian Society in 1829. The *London Medical Gazette* in that year described it as follows: " It consisted of an oblong piece of looking-glass set in a silver wire with a long shank. The reflecting part is placed against the palate, whilst the tongue is held down by the spatula, when the epiglottis and the upper part of the larynx becomes visible in the mirror." Babington called his invention the " glottiscope ". The term " laryngoscope " appears to have been coined by his friend Hodgkin. There is evidence to show that Babington continued to use his laryngoscope for many years, but he did not publish any report on the subject. Similar instruments were described by Baumès of Lyons (1838), Liston (1840), Avery (1844), and Türck of Vienna and Czermak of Pesth (1857). In 1855 Garcia presented his famous paper to the Royal Society. Garcia's report created little interest in London, but the possibilities of his instrument were quickly realized by Türck and Czermak, and it was the latter who introduced the modern frontal mirror and so solved the problem of adequate illumination. Although Garcia is now generally regarded as the father of laryngoscopy, there is no

doubt that Babington's priority was recognized by his contemporaries. Babington must have known of Garcia's work, but his extraordinary diffidence prevented him from making any claim on behalf of his own earlier communication. Perhaps a second reason for the neglect of Babington's work was his great versatility. He invented the term *liquor sanguinis* for the fluid part of the blood, and his description in 1865 of hereditary haemorrhagic telangiectasia long antedates the observations of Rendu (1896) and Osler (1901). Babington was equally distinguished as Oriental scholar, linguist, poet, haematologist, biochemist, clinician, and epidemiologist (besides showing considerable talent in painting and sculpture), but himself attached little importance to his various pieces of work, any one of which would have sufficed to make the reputation of a lesser man.

W. J. Bishop

598. **Lady Holland's Atheist. John Allen, M.D. (1771–1843)**
B. HILL. *Practitioner* [*Practitioner*] **170**, 175–180, Feb., 1953. 1 fig.

599. **The Charitable Institutions of Ancient Rome.** (Le istituzioni di beneficenza nell'antica Roma)
E. MARINUCCI. *Difesa sociale* [*Difesa soc.*] **4**, 33–45, Oct.–Dec., 1952. 16 refs.

In the earlier periods of Roman history there were no charitable organizations, and the virtue of charity was not cultivated. In the later Republic and the Empire they were numerous, as is testified by the literature, laws, inscriptions, and bas-reliefs of the period. The teaching of Seneca and the Stoics, as well as the influence of the Christians—especially that of St. Paul—provided a congenial atmosphere for the spread of humanitarian activities.

Even under the Republic, part of each temple of Aesculapius was set aside for the sick poor and the slaves, although, of course, these temples were not nearly so numerous as in Greece. Then, under the Empire, the needs of the poor and the aged were recognized by the free distribution of corn, and later of oil, wine, meat, and clothes. There were many charities founded especially for the protection and care of children, and Trajan was noted for his encouragement and support of this cause. Every township had its special chest, the *arca alimentaria* presided over by *curatores*, corresponding to the modern system of relief administered by "guardians". After the fall of Rome, the Christian church took over this work from the State.

F. N. L. Poynter

600. **Mediaeval "Leprosy" in the British Isles**
W. MACARTHUR. *Leprosy Review* [*Leprosy Rev.*] **24**, 8–19, Jan., 1953.

It is quite certain that leprosy existed in Britain in the Middle Ages, but it is difficult to arrive at any true estimate of the prevalence of the disease because of the different meanings attached to the word "leprosy" in the past. The term leprosy was applied to the true disease and to every malady that was thought to be leprosy. The Greek form *lepra* (*leprós*, scaly) was used by the Greeks themselves for scaling skin diseases of the psoriasis type but never for leprosy, for which they used the word "elephantiasis" because of the thickening and corrugation of the skin. "Lepra" was, however, adopted as the classical medical term for leprosy, and it was also applied to a number of skin conditions associated with scales or scabs, and even to epidemic diseases like smallpox and the Black Death (bubonic plague). "Leprous" sometimes implied nothing more than weak and infirm, and "leprosus" could mean simply a beggar. The numerous biblical references to leprosy kept the word for ever in people's minds. Job was pronounced a leper, and the beggar at the rich man's gate was supposed to be suffering from the disease, although the Biblical record makes no mention of leprosy. The name Lazarus, which means no more than "without help", became a synonym for his supposed disease, and still survives in the terms "lazar" and "lazar house".

In the 12th century the Church did much to arouse sympathy and help for lepers. Leper houses were founded up and down the country, but there has been some misunderstanding of their purpose and function, and gross exaggeration of their numbers. Although the disappearance of leprosy in Britain is often attributed to strict segregation of lepers, there is little evidence to show that they were cut off from the community. There is no contemporary evidence that the so-called "leper-squints" in churches had anything to do with the disease. The only statutory measure directed against lepers is said to have been the writ *De leproso amovendo*, which, however, had only a very limited application and expressly laid down that a leper or lazar was not to be moved out of his house so long as he did not converse with his neighbours. In some leper houses the inmates were allowed to receive friends, and in some codes of rules the final penalty for contumacious behaviour was expulsion. Lepers had a right to beg, a concession which must have given great encouragement to imposters. That lepers were accustomed to roam about can be inferred from an edict of 1346 expelling all the lepers residing in London. The number of leper houses in England has been given as 283, but no such number can have been in active operation at any one period. Some alleged lazar houses were almshouses; many became derelict and their endowments were put to other uses; some are known only from single references in wills and other documents and little can be learned of their history. The celebrated Leper Hospitals of Armagh are shown to be entirely mythical and to owe their reputed origin to mistranslation of a word in an old Celtic chronicle. The question whether Robert the Bruce was a leper is considered at length, and the author concludes that the imputation is quite false. No assertion of leprosy in olden times can be accepted unless there is sufficient clinical detail to point the diagnosis. The most reasonable estimate of the actual prevalence of leprosy in mediaeval England is that of Creighton, who says: "There may have been a leper in a village here and there, one or two in a market town, a dozen or more in a city, a score or more in a whole diocese."

W. J. Bishop

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